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THE PROTEAN CHARACTER OF THE LEUKEMIAS AND OF THE LEUKEMOID STATES*

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THE classic features of both the acute and the chronic leukemias are well known to all, and lead in the majority of cases to a correct diagnosis and thus to appropriate treatment and accurate prognosis. There are, however, certain deviations from the usual picture which, though uncommon, are of practical importance because of their diagnostic, therapeutic or prognostic implications. Not all patients having the peripheral blood picture of leukemia actually suffer from that disease; not all cases of leukemia present, in the early stages of their disease at least, those features by which we are accustomed confidently to diagnose the condition. It is our present purpose to describe briefly some of these borderline cases.

It is generally agreed that, on the average, the chronic leukemias, whether myelogenous or lymphatic, terminate fatally in about three years from the onset of symptoms.[1] All too frequently, the course is even more rapid. Yet there are, rarely, notable exceptions to this general rule, and these very exceptions should render us cautious in our initial prognosis, particularly when the patient is relatively symptom-free at the time the condition is discovered. Some 10 per cent of patients with chronic leukemia, whether lymphatic or myelogenous, survive more than five and up to ten years.[1] Very rarely they live even longer.

Case 1. I. E., a 69-year-old woman, complained early in 1929 of lassitude, loss of strength and generalized aches and pains. There were no more specific symptoms. On examination she was found to be a frail woman, older than her years would indicate. The lungs were clear; the heart was normal. There was moderate arteriosclerosis. The spleen was felt 2 cm. below the costal margin; the liver was just palpable on inspiration. There was slight generalized lymphadenopathy. Otherwise the physical examination was essentially normal. The red-cell count was 4,800,000 and the hemoglobin 85 per cent. The white-cell count was 59,000, with 99 per cent mature lymphocytes. The platelets were present in normal numbers. By all criteria the patient had chronic lymphatic leukemia and death would have ensued within the next 2 or 3 years, if one were guided by the general averages which apply to this disease. Yet her condition has remained essentially unchanged to the date of writing. From time to time she has been given high-voltage x-ray therapy over the splenic area. Her weakness has continued, and indeed increased; her strength has gradually failed, yet in May, 1938, 9 years after onset, the red-cell count was 4,100,000 and the white-cell count was only 16,800, with 72 per cent mature lymphocytes, 20 per cent mature polymorphonuclears and 8 per cent monocytes. Senility seems to be increasing, yet the leukemia remains essentially unaltered; indeed, it can hardly be said to have contributed in any important manner to her present state.

Case 2. F. B. M., a 42-year-old man, noticed in 1926 a generalized, painless lymphadenopathy; otherwise he felt perfectly well. Physical examination showed great enlargement of the lymph nodes in the neck, axillas and groins. The nodes were rubbery in consistence, discrete and freely movable. They varied in size but averaged about 4 cm. in diameter. The spleen reached nearly to the iliac crest. The liver could not be felt. The white-cell count was 186,000, with 93 per cent mature lymphocytes and 7 per cent polymorphonuclear neutrophils. The red-cell count was 4,350,000. The general condition was good and there were no complaints besides the enlarged lymph nodes, which caused him some worry and were naturally disfiguring. From time to time since 1926 he has received x-ray therapy over the splenic area and the enlarged lymph nodes. With each treatment the white-cell count has fallen markedly, only to rise once more in a few months to its previous level. The lymph nodes have fluctuated in a similar manner. The spleen has remained consistently large; indeed, it has always been of unusual size for a case of lymphatic leukemia. In May, 1938, 12 years after onset of his illness, the patient still showed marked lymphadenopathy. The white-cell count was 138,000, with 97 per cent mature lymphocytes. The red-cell count was 4,300,000 and the hemoglobin 85 per cent. Blood platelets were present in normal numbers. The spleen still reached to the iliac crest, but the patient was in excellent general condition, and was able to carry on an active and profitable insurance business.

The most protracted case we are aware of was observed by McGavran.[2] We have reviewed the autopsy material from this case and there can be no question as to the correctness of the diag-

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nosis. The patient, F. C., a forty-eight-year-old man, was found on routine examination in 1911 to have a white-cell count of 232,000, with 93 per cent mature lymphocytes. The red-cell count and hemoglobin were normal. He had very mild diabetes, but presented no symptoms suggestive of leukemia. It is impossible to say how long his blood condition had already existed before it was discovered. No specific therapy was instituted. The patient continued to show the characteristic signs and the hematologic picture of lymphatic leukemia, but remained essentially symptom-free until 1926, when he began to lose weight and suffer from intractable diarrhea. It was correctly surmised that these symptoms were traceable to his fundamental blood disorder. X-ray therapy promptly relieved the diarrhea and greatly improved the general condition. At about the same time, however, he began to complain of angina pectoris. Gradually his heart condition became worse and he died in 1935 of coronary thrombosis, twenty-four years after his leukemia had been discovered. Autopsy revealed the characteristic leukemic infiltration of the liver, spleen, lymph nodes and bone marrow.

It may be argued that these patients did not, in actuality, have lymphatic leukemia; that their life span was inconsistent with such a diagnosis. Yet it must be admitted that throughout life they showed the signs, symptoms and laboratory findings usually considered diagnostic of that condition; furthermore, in the case just described, postmortem examination revealed the essential findings of that disease with splenomegaly, hepatomegaly and generalized leukemic infiltration of the bone marrow.

From time to time, therefore, one encounters patients who by all known criteria appear to have the disease we call leukemia, but who, for reasons as yet unknown, live in comparative comfort far beyond the usual duration of this condition. Such patients are usually relatively symptom-free early in the course of their illness, and not infrequently physical examination reveals few abnormalities. Most commonly these cases have lymphatic leukemia, much more rarely myelogenous leukemia. So far as our experience goes, monocytic leukemia is never of long duration.

Unfortunately we may also err in our prognosis in the opposite direction. Leukemic patients apparently in good condition may be struck down suddenly and death may ensue rapidly when but a short time before one would have said, and with some justification, that the immediate outlook was good. We do not refer to a rapidly fatal outcome due to other pathologic conditions, but to that directly traceable to the leukemic state.

Case 3. N. S., a 30-year-old woman, had been known to have myelogenous leukemia for over a year. Under x-ray therapy her initial symptoms, — abdominal distress after meals and weakness, — had abated and her white-cell count, previously 150,000, had fallen to 12,200. The differential at various times had shown from 20 to 40 per cent myelocytes. The red-cell count had fluctuated between 4,500,000 and 5,000,000. The platelets had gradually diminished from normal to approximately 80,000 per cubic millimeter. The patient's general condition, however, seemed excellent, and she was able to carry on an active career provided she rested for an hour or so after lunch each day. There was no anemia or lymphadenopathy, and the spleen was just palpable on inspiration. One morning she complained of vertigo, extreme weakness and chilliness. Physical examination revealed a very apprehensive woman with a pulse of 160, respirations of 40 and a temperature of 105°F. The lungs were clear. The peripheral blood picture did not differ materially from that which had obtained during the previous months. She was slightly disoriented and so dizzy that she was unable even to sit up in bed. She became increasingly incoherent, disoriented and drowsy and died the next morning, presumably from a massive cerebral hemorrhage, possibly of the intraventricular type. There is every reason to believe that the hemorrhage was directly due to the leukemia.

Case 4. L. W., a 49-year-old man, entered the hospital complaining of slight weakness of 1 month's duration and a mass in the abdomen. Physical examination revealed a spleen which reached to the level of the umbilicus, and the patient proved to have myelogenous leukemia, with a white-cell count of 27,000 and a differential count of 40 per cent mature polymorphonuclear neutrophils, 16 per cent metamyelocytes and 20 per cent myelocytes. The red-cell count was 3,800,000 and the platelets were considerably reduced in number. The general condition was good and the prognosis was considered favorable, chiefly on account of the comparatively small percentage of immature white cells in the blood and the paucity of the symptoms. On the 3rd day, before receiving any x-ray therapy, the patient passed a large amount of blood by rectum and died a few hours later. Autopsy revealed the characteristic findings of myelogenous leukemia and no cause of death other than the massive intestinal hemorrhage, probably dependent on the hemorrhagic diathesis incident to leukemia.

In all instances the patient's family should be advised of the fact that sudden death may occur even though the patient seems to be progressing satisfactorily.

The acute leukemias frequently present greater diagnostic problems than do the chronic forms. The usual picture of weakness, fever, moderately elevated white-cell count, grossly abnormal differential count with many primitive cells of one series or another, progressive anemia and thrombocytopenia may be very incomplete or even entirely lacking early in the disease. Any one of these features may fail to appear until comparatively late. In short, the blood findings may reflect but poorly the underlying pathologic condition and unless one bears this fact constantly in mind, serious errors are liable to be made.

Case 5. C. P., a 65-year-old woman, complained in early December, 1935, of weakness and easy fatigability. The previous June she had had a short attack of fever of uncertain origin, accompanied by a moderate lymphocytosis and an enlarged and tender lymph node in the left axilla. From this indefinite illness she had recovered rapidly and completely. In December, she complained of weakness and was found to be running a septic type of temperature ranging at night from 99 to 102°F. Her appetite was poor. On one occasion she vomited a little blood. A few days later she passed a small amount of dark blood by rectum. Physical examination was essentially normal except for a moderate degree of loss of weight, some tenderness low in the left flank and a distended abdomen. There was no lymphadenopathy; neither the spleen nor liver was palpable. The lungs were clear and the heart appeared normal. The red-cell count was 4,210,000 and the white-cell count 10,200, with 11 per cent mature polymorphonuclear neutrophils, 22 per cent immature polymorphonuclear neutrophils, 13 per cent metamyelocytes, 10 per cent myelocytes, 36 per cent lymphocytes and 8 per cent monocytes. The platelets were present in normal numbers. It was suspected that the patient had some obscure infection or a carcinoma of the gastrointestinal tract. She gradually failed without developing any specific or localizing symptoms or signs and died December 27. Autopsy revealed the classical picture of aleukemic myelosis — namely a replacement of the normal marrow elements by stem cells and myeloblasts. There was no leukemic infiltration of the liver, spleen or lymph nodes. During life one could not properly have diagnosed leukemia. Yet the patient died of that disease (or at least one closely allied to it) within 4 weeks from the onset of symptoms.

The diagnostic difficulties become still greater when some other specific disease is more or less closely simulated or when the presenting symptom is such that one's attention is distracted from the underlying blood dyscrasia.

Case 6. C. C., an 8-year-old girl, complained in June, 1932, of migratory joint pains in the ankles, wrists and elbows. She was found to be running a slight, irregular temperature. The involved joints were swollen, tender and very painful on active or passive motion. There was a soft systolic apical murmur. Otherwise the physical examination was normal. A diagnosis of rheumatic fever was made, and under salicylate therapy the patient improved rapidly; she remained apparently well until August of the same year, when there was a recrudescence of the joint pains and marked loss of weight and strength. The red-cell count was 2,300,000, the hemoglobin 50 per cent, and the white-cell count 400, with 2 per cent polymorphonuclear neutrophils and 98 per cent lymphocytes. The platelets were normal in number. Several blood transfusions were given and the red-cell count rose to 5,000,000 and the white-cell count to 7000, with 66 per cent polymorphonuclear neutrophils, 33 per cent lymphocytes and 1 per cent monocytes. The arthritic pains, however, continued unabated and the child failed rapidly. From the end of August occasional myelocytes and stem cells appeared from time to time in the blood smears, and the platelets fell progressively reaching 20,000 per cubic millimeter on October 10. An x-ray taken shortly thereafter showed fine mottling of the cranial bones and of the pelvis. In addition the long bones showed generalized absorption, most marked at the ends, giving the appearance of rotten wood. On the basis of the clinical picture together with the x-ray findings, the presence of thrombopenia and occasional very immature white cells in the blood smear, a diagnosis of leukemia was made; it was confirmed by bone-marrow biopsy. From then on more and more stem cells appeared in the blood stream, and by January 26, 1933, the red-cell count had fallen to 1,500,000. The white-cell count was 700, with 24 per cent mature polymorphonuclear neutrophils, 2 per cent young polymorphonuclear neutrophils, 6 per cent myelocytes, 40 per cent stem cells and 28 per cent lymphocytes. The patient died shortly thereafter. The diagnosis had for several months been very much in doubt and leukemia was not seriously considered until comparatively late in her disease. Yet there can be but little doubt that it was already well advanced when medical care was first sought, and that the initial "arthritic pains" were in reality due to the same leukemic destruction of the bones that became so prominent a feature of the later illness.

"Arthritic pains" are a not uncommon complaint in children with acute leukemia;[3, 4] in adults they are rarely encountered. The x-ray picture is very characteristic, presenting as it does a moth-eaten or mottled appearance, particularly at the ends of the long bones; periosteal elevation is common; and in conjunction with an abnormal blood in which are found myelocytes and stem cells, be they ever so few in number, the diagnosis of leukemia can be made with some confidence.

Occasionally acute leukemia may start with the signs and symptoms of an acute abdominal emergency.

Case 7. T. F., a 4-year-old boy, was awakened early one morning by severe pain in the right lower quadrant. His doctor found marked tenderness and spasm at McBurney's point, a moderate elevation of temperature and a white-cell count of 18,000. A tentative diagnosis of appendicitis was naturally made and operation was deemed necessary. At the hospital the differential white-cell count showed practically 100 per cent stem cells. Nevertheless, the boy was operated on and the appendix was found to be infiltrated by leukemic cells. Immediate convalescence was uneventful and the patient was discharged on the 10th hospital day, but anemia, hepatomegaly and splenomegaly rapidly developed and he died 2 months after the apparent onset of his condition. He had entered the hospital with an entirely justifiable diagnosis of acute appendicitis, with all the prognostic implications of that condition. He left 10 days later doomed to certain death.

Case 8. R. M., a robust and active man of 51, was seized with extreme pain in the lower abdomen and presented all the signs of complete intestinal obstruction. There was no fever. He was immediately operated on, but no obstruction was found. Both liver and spleen were moderately enlarged. There was no lymphadenopathy. Postoperatively the red-cell count was 5,200,000, the hemoglobin 102 per cent and the white-cell count 1000, with 100 per cent stem cells. The platelets were greatly reduced. The patient developed a moderate degree of fever and slight jaundice. There was pronounced enlargement of the salivary glands and lymph nodes in the neck. For a few days there was rapid improvement and the white-cell count rose to 21,000, with a practically normal differential count. Equally rapidly, however, the immature cells reappeared, and 6 days after entry stem cells consti-

tuted 87 per cent of the total white cells. At that time the spleen reached to the umbilicus. The patient died 8 days after his operation. Postmortem examination showed the characteristic findings of acute myelogenous leukemia with infiltration of the liver, spleen, kidneys, intestinal wall and bone marrow.

In the vast majority of instances, once the diagnosis of acute leukemia is established the patient grows steadily worse and responds but little to any therapeutic measure. Occasionally the condition progresses by a series of minor remissions and relapses without there being at any time any question of the correctness of the original diagnosis. In rare cases there occur frank remissions of considerable duration, during which few if any features of leukemia are present and in which the patient returns to apparently excellent health, and unless this fact be borne in mind, serious errors may be made.[5] The original diagnosis may be doubted or even discarded and both the doctor and the family may be lulled into a false sense of security which is in no way justified by the subsequent course.

Case 9. J. R., a 35-year-old butcher, entered the hospital November 9, 1929. A week before entry he had become very weak and had profuse bleeding from the gums. Fever was noted from the onset. The day before entry a small quantity of fresh blood was passed by rectum. Physical examination showed a pale, prostrated man with greatly swollen and bleeding gums. There were many bean-sized lymph nodes in each side of the neck. The spleen reached to the level of the umbilicus. In the lower rectum could be felt an exquisitely tender mass which bled freely on gentle palpation. The temperature was 100°F. On the day of admission, his red-cell count was 3,120,000 and the hemoglobin 70 per cent. The white-cell count was 11,000, with 90 per cent stem cells, 4 per cent polymorphonuclear neutrophils and 6 per cent lymphocytes. No platelets were seen in the smear. Two days later petechiae appeared in profusion over the neck, shoulders and chest. The temperature rose to 105°F. and the patient seemed moribund. The white-cell count fell to 2800, with the differential count essentially unchanged. Within the next few days, however, the count rose precipitately and the differential white count steadily approached normal, the stem cells being gradually replaced first by myelocytes, then by metamyelocytes and finally by mature polymorphonuclear neutrophils. The platelets increased rapidly. The patient gained in strength; the temperature fell to normal; the bleeding ceased, the spleen receded to normal size and the enlargement of the cervical lymph nodes completely disappeared. By December 18, 1 month after entry, the white-cell picture was entirely normal, blood platelets were present in the usual number and the general condition was excellent. The red-cell count gradually rose to 5,000,000. During January, February, March and April, the patient was perfectly well in all respects. The physical examination was normal and no abnormalities could be detected in his peripheral blood. No trace of the fulminating disease from which he had suffered in November remained. Suddenly in late April, he was seized with a severe headache. Once more he was found to have the characteristic blood picture of acute leukemia (only 3 days previously the blood smear had been entirely normal) and he died May 5, 5½ months from onset, after a complete remission of nearly 5 months. A bone-marrow biopsy shortly before death revealed the characteristic histologic picture of acute myelogenous leukemia.

What caused the remission? What relation had the first illness to the second? Was the patient temporarily cured of his leukemia, or was it merely that the outward and visible signs of the disease were no longer manifest? These questions cannot at present be answered. But we do know that such remissions occur, and it is obvious that their appearance may cause great confusion, particularly if in the first attack there has been any doubt regarding the diagnosis; we have already seen that in the initial stages of acute leukemia the signs and symptoms may be far from pathognomonic.

Case 10. N. B., a 5-year-old girl, became ill in November, 1932. She ran a septic temperature reaching to 102°F. and became rapidly weaker. The red-cell count on admission to the hospital was 2,000,000. The hemoglobin was 36 per cent and the white-cell count was 13,000, with 9 per cent polymorphonuclear neutrophils, 86 per cent lymphocytes and 5 per cent myelocytes. After 1 month she contracted measles and developed bilateral otitis media and necrosis of the lower lip. The white-cell count fell to 1000 and the differential white-blood count showed 91 per cent immature lymphocytes. The platelet count dropped to 10,000 and the red-cell count fell to 1,200,000. After several blood transfusions and intensive Pentnucleotide therapy the white-cell count rose to 10,200 with a normal differential count, and the red-cell count rose to 4,200,000 early in January, 6 weeks after the initial symptoms. In the meantime the temperature fell to normal, the otitis cleared up and the patient's strength completely returned. She remained entirely well both from a clinical and hematological point of view until May 16, 1933, when she developed bilateral mastoiditis, with a temperature of 105°F. In addition she had generalized joint pains, and x-ray studies revealed the characteristic picture of leukemic infiltration of the bones, just as in Case 6. The red-cell count was 1,800,000 and the white-cell count 23,000, with 97 per cent immature lymphocytes. During the next 6 weeks the patient failed rapidly, and she died in mid July, 8 months after her first illness and 10 weeks after the termination of the 5-month remission. Postmortem examination showed the characteristic features of acute lymphatic leukemia.

Here again we have an example of a dramatic remission after an illness which had all the hallmarks of acute leukemia. As has been said, we are ignorant of the cause of these remissions, but it is important to recognize that they may occasionally occur. In our experience, they usually follow a definite pattern. After a stormy onset, the elevated white-cell count falls rapidly to well below normal, then as rapidly rises once more. The immature white blood cells, initially present in large numbers, become less and less. With the rising white-cell count the differential count becomes steadily more normal. During this time the patient's general condition improves rapidly

and the red-cell count, which has been steadily falling, rises rapidly to a normal value. The platelets return and the patient appears to have recovered. After a period of one to five months all the signs and symptoms of acute leukemia suddenly reappear, and the patient dies in a comparatively short time.

Patients may present a peripheral blood picture indistinguishable from that of leukemia yet actually suffer from some entirely different disease, and occasionally one which does not run the fatal course of that condition. It is well known that in sepsis there is frequently a marked shift to the left in the white-cell picture. It is not so generally appreciated that the blood may be indistinguishable from that in leukemia.[6] In patients who are recovering from agranulocytosis and in whom considerable sepsis exists, one may find white-cell counts as high as 155,000, with myelocytes as high as 45 per cent. Under these circumstances it is easy to regard the initial illness as an atypical aleukemic leukemia, and to see in the subsequent elevated white-cell count and the grossly abnormal differential count positive evidence for the leukemic state with its inevitably fatal outcome. In 1 case after an acute agranulocytosis the temperature, which had become normal, started to rise again, the white-cell count rose to 33,000 and the differential count showed 42 per cent early myelocytes. Sepsis was suspected, but on account of the white-cell picture the physician in charge of the case insisted that the condition was leukemia. The patient died of a brain abscess secondary to an unrecognized orbital cellulitis, and postmortem examination failed to reveal any signs of leukemia. Aleukemic leukemia may also be simulated.

Case 11. J. G., a 45-year-old man, was admitted to the hospital July 17, 1937. For 1 week he had had symptoms consistent with a diagnosis of pneumonia—pain in the chest, fever, cough and blood-streaked sputum. No blood examination had been made.

Physical examination on entry revealed a semicomatose man with a slight jaundice. There were indefinite signs of pneumonia at the right base. The liver was felt 4 cm. below the costal margin. The spleen was easily palpable. The temperature was 104.4°F., the pulse 130 and respirations 28. The red-cell count was 4,000,000, the hemoglobin 75 per cent and the white-cell count 1000, with 23 per cent polymorphonuclear neutrophils, 19 per cent metamyelocytes, 33 per cent myelocytes, 14 per cent stem cells and 11 per cent lymphocytes. The platelets were markedly diminished. A diagnosis of myelogenous leukemia with complicating pneumonia was made. The patient died within 24 hours. Postmortem examination showed lobar pneumonia of the right lower lobe, alcoholic cirrhosis and a hyperplastic bone marrow. There was no evidence of leukemia.

These diagnostic difficulties are materially increased when one remembers that patients who have had undoubted leukemia, as proved by blood studies and bone-marrow biopsy, may die shortly thereafter and at autopsy show not the slightest evidence of the disease.

Case 12. J. T. H., a 68-year-old man, was admitted to the hospital on October 14, 1929, with the chief complaint of a mass in the left upper quadrant. In addition he had some pain in the region of the mass. Physical examination revealed the spleen descending to the level of the umbilicus and the liver could be felt 8 cm. below the ribs. Otherwise the examination was essentially normal. The red-cell count was 3,370,000, the hemoglobin was 68 per cent and the white-cell count was 275,000, with 50 per cent polymorphonuclear neutrophils, 42 per cent neutrophilic myelocytes, 3 per cent eosinophilic myelocytes and 5 per cent stem cells. The basal metabolic rate was +46 per cent. The patient was given x-ray therapy with a moderate drop in the white-cell count and a definite though not marked diminution in the size of the spleen. He gradually failed. One month after admission the red-cell count had fallen to 2,700,000, the hemoglobin to 50 per cent and the white-cell count to 5250. The differential had become essentially normal and the basal metabolic rate had dropped to +4 per cent. The patient died January 26, 1930. Postmortem examination failed to show any infiltration of the liver or spleen. In most places the vertebral bone marrow was completely fatty, and here and there could be seen small areas characteristic (in so far as the particular field was concerned) of leukemia. For the rest, all evidence of the disease had disappeared.

In this case there was no bone-marrow biopsy at entrance to prove the condition, but the elevated metabolism and the occasional leukemic patches in the marrow virtually prove that the patient did in fact have leukemia, and that that disease had given way to aplastic anemia. Mallory[8] reports an almost identical case in which a bone-marrow biopsy confirmed the leukemic infiltration occurring early in the course of the disease.

Many other pathologic states may give rise to blood pictures indistinguishable from that of leukemia.[6] We draw special attention to two, namely miliary tuberculosis and carcinoma.

Case 13. F. K., a 19-year-old man, entered the hospital with a history of weakness and fatigue for 2 months. The temperature was 104°F., the pulse 120, and the respirations 25. Physical examination showed very marked pallor of the mucous membranes and bean-sized lymph nodes in each side of the neck, each axilla and each groin. The spleen was easily palpable on deep inspiration. The red-cell count was 2,130,000, the hemoglobin 49 per cent and the white-cell count 6100, with 44 per cent polymorphonuclear neutrophils, 25 per cent myelocytes, 22 per cent myeloblasts, 8 per cent lymphocytes and 1 per cent monocytes. The platelet count was 187,000. The patient continued to run a septic temperature with occasional chills. Blood cultures were repeatedly negative. During the next 2 months he sustained numerous superficial skin abscesses and was regarded as having a subacute myelogenous leukemia with sepsis. The red-cell count fell to 1,900,000, the white-cell count to 2100, with 33 per cent myeloblasts, and the platelet count to 46,000. The physical examination remained essentially as on admission. The patient died

5 months from the onset of his illness, and postmortem examination showed widespread miliary tuberculosis of the lungs, pleura, lymph nodes, spleen, liver and bone marrow. There was no evidence of leukemia.

In certain cases carcinoma may give rise to a blood picture closely simulating leukemia — and this without necrosis, infection or fever.

Case 14. M. M., a 70-year-old woman, was admitted to the hospital with a story of cough and increasing weakness for 4 months. In addition she had been losing weight rapidly. Her past history was essentially normal except that for 10 years she said she had "glands" in her neck.

Physical examination showed a frail, elderly woman. The thyroid was definitely enlarged, nodular and firm. The liver was palpable 4 cm. below the costal margin. Otherwise there were no notable abnormalities. The temperature was normal, the respirations were 30 to 35 and the pulse was 110 to 130. On entrance the red-cell count was 4,300,000, the hemoglobin 85 per cent and the white-cell count 76,000, with 85 per cent polymorphonuclear neutrophils, 12 per cent myelocytes, 2 per cent lymphocytes and 1 per cent monocytes. The platelets were diminished in number. During the next few days, the white-cell count rose to 180,000, with increasing numbers of early myelocytes, and the patient died on the 4th day. At no time did her temperature rise above normal. Postmortem examination showed slight bronchopneumonia, colloid adenoma of the thyroid and a large mediastinal carcinoma with metastases to the liver and spleen. The bone marrow showed increased activity in both red-cell and white-cell series, but no leukemic infiltration.

The following case was still more striking.

*Case 15.** I. R., a 45-year-old carpenter, developed a cough and pain in the chest 6 weeks before admission to the hospital. Physical examination on entrance was essentially normal except for slight dullness at the right apex of the lung, associated with increased tactile fremitus and slight dullness in the right lower axilla. The red-cell count was 4,300,000, the hemoglobin 80 per cent and the white-cell count 51,250, with 85 per cent polymorphonuclear neutrophils, 11 per cent lymphocytes, 2 per cent monocytes, 1 per cent eosinophils and 1 per cent basophils. The patient's temperature fluctuated between 98 and 100°F. Two weeks later the patient experienced a sudden, sharp, severe pain in the left axillary region and immediately coughed up a large amount of foul, blood-tinged sputum. Although the red-cell count remained normal the white-cell count rose to 116,000, with 93 per cent polymorphonuclear neutrophils, many of which were band forms. A lateral chest film showed an oval area of consolidation in the central part of the right lung field. The cough, sputum and fever continued and the patient gradually failed and died 2 months after his initial symptoms. Postmortem examination showed a carcinoma of the right lung with metastases to the regional lymph nodes, liver, pancreas, adrenals and kidney. The bone marrow was so hyperplastic as to resemble superficially that seen in leukemia. But the percentage of immature granulocytes in the marrow was no greater than normal, the hyperplasia was patchy rather than diffuse and there was no leukemic infiltration in the liver, spleen or lymph nodes.

The method by which such gross hyperplasia is produced in the presence of carcinoma (especially of the lung and of the liver, it would seem) is uncertain; but the fact remains that malignant disease may produce a leukemoid blood picture and, as in the case just cited, may result in a degree of bone-marrow hyperplasia superficially resembling that seen in leukemia.

Finally, we wish to refer to that pathologic state which for lack of a better term is now called myeloid metaplasia, a condition which closely simulates leukemia both from a clinical and a hematological point of view, but which runs a more benign course. Its etiology and indeed its pathogenesis is obscure. It would seem probable, however, that for a variety of reasons — abnormal blood supply to the bone marrow, fibrosis of the marrow, osteosclerosis or the like — the normally active and efficient hematopoietic tissues are no longer able to carry on their allotted function and the normally fatty marrow of the femur and tibia, together with the potentially hematopoietic organs such as the liver and spleen, must perforce take over the task of producing the blood cells so necessary for the bodily economy. That these newly called upon tissues are but poor successors to the "red marrow" is attested by the peripheral blood picture, which is, as has been said, leukemoid in type.

Case 16. L. J., a 51-year-old married woman, entered the hospital on September 28, 1931. Twenty-five years previously she had had a severe attack of jaundice with headache, nausea, vomiting and vertigo. Since that time she had had three similar attacks, the last one in 1923. In 1926 an abscessed tooth was removed and there followed profuse bleeding for 24 hours. A few weeks after this episode there was a "massive hemorrhage" from the mouth and much blood was found in the stools. An abdominal exploration was performed and a gastric ulcer was said to have been found, although the evidence on this point is not entirely clear. In 1929, the patient's tongue became sore and she lost considerable weight. During the next few years she felt below par; her appetite was poor and she continued to lose weight. Physical examination on entry showed an atrophic tongue, slight pallor of the mucous membrane and a spleen extending 4 cm. below the ribs. Otherwise there were no noteworthy abnormalities. There was no free hydrochloric acid in the stomach, even after histamine. The red-cell count was 5,390,000, the hemoglobin 57 per cent and the white-cell count 28,500, with 70 per cent polymorphonuclear neutrophils, 9 per cent myelocytes, 11 per cent lymphocytes, 3 per cent monocytes, 4 per cent eosinophils and 3 per cent basophils. The platelets were not only unusually large but greatly increased in number. The reticulocytes were 2.8 per cent, the icteric index 7.0 and the fragility of the red cells normal. A tentative diagnosis of early myelogenous leukemia was made and the patient was given iron by mouth. Within 1 month the red-cell count had risen to 7,000,000 and the hemoglobin to 68 per cent. The patient felt well, but several ecchymoses appeared on each thigh. During the next 6 months the condition remained essentially unaltered and the red-cell count at 7,000,000 or slightly above. In March, 1933, a sternal-bone-marrow bi-

*I am indebted to Dr. Tracy B. Mallory, of the Massachusetts General Hospital, for permission to cite this case.

opsy showed that in this region at least the normal elements had been completely replaced by fibrous tissue.

During the ensuing months the red-cell count gradually fell to normal, and it remained at that level from September, 1933, to June, 1938. The hemoglobin dropped gradually from 110 per cent on December 9, 1931, to 52 per cent in June, 1938. The white-cell count fluctuated between 9000 and 28,000, and at all times the differential count showed a definite and increasing percentage of immature cells of the granulocyte series. During 1931 and 1932 the polymorphonuclear neutrophils had varied from 69 to 89 per cent and the myelocytes from 1 to 10 per cent. Basophils were constantly present, and varied between 2 and 5 per cent. By 1934 there were almost constantly present more than 12 per cent myelocytes, and a few nucleated red-blood cells were seen from time to time.

Early in 1938, when the red-cell count had dropped to 3,460,000 and the hemoglobin to 49 per cent, the white-cell count was 18,750 and the differential count showed 42 per cent polymorphonuclear neutrophils, 25 per cent myelocytes, 5 per cent stem cells, 10 per cent basophils and 18 per cent lymphocytes. Seventeen nucleated red cells were seen while counting 100 white cells. The platelet count was 180,000. The blood picture was essentially that of an early myelogenous leukemia. At this time the patient was definitely weaker than ever before. She had lost much weight; the liver reached nearly to the umbilicus and the spleen nearly to the iliac crest.

The basal metabolic rate was +20 per cent, a rate entirely consistent with the degree of myeloid metaplasia which the patient was assumed to have, but rather lower than that which would probably have obtained in chronic leukemia of this duration and activity.

A second bone-marrow puncture was done, and again it showed merely fibrosis of the marrow. In view of the long, relatively asymptomatic course, the initial polycythemia and the bone-marrow findings, one must conclude that the condition was one of myeloid metaplasia rather than myelogenous leukemia, as was originally suspected.

CONCLUSION

It is apparent from a consideration of these cases that the course of the various leukemias may deviate sharply from the classic one; on the other hand, various other pathologic conditions — some of them curable — may give rise to a blood picture indistinguishable from that seen in this disease.

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HYPERHIDROSIS OF NERVOUS ORIGIN AND ITS TREATMENT BY SYMPATHECTOMY*

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BOSTON

LIST and Peet,[1] in their excellent articles on the activity of the sweat glands, have shown that these structures respond both to thermal and to psychic stimuli. While heat sweating is a generalized process and is rarely a cause for complaint, hyperhidrosis of nervous origin may become extremely annoying and even incapacitating. The latter variety is usually limited to the palmar and plantar surfaces and to the fingers and toes. Above the wrists and ankles perspiration is normal (Fig. 1). The clamminess of hands and feet may be really disabling. Beads of perspiration may form on the fingertips and wet everything the patient handles. Shaking hands may become most embarrassing; as one of my patients, a lawyer, complained: "The law is a handshaking profession and I can't do it!" Another patient, a medical student, could not assist at operations because the sweat ran over the tops of his rubber gloves. The feet commonly perspire to a similar extent, so that the lower part of the sock or stocking is dripping wet. The feet of one of Telford's[3] patients sweat so excessively that he was forced to take off his boots and empty them of water several times a day. Excellent photographs of the excessive degree of sweating which may be seen in this condition are to be found in an article by Adson, Craig, and Brown.[4]

This type of hyperhidrosis is usually accompanied by some degree of vasospasm, so that the sweaty extremities are frequently cold and at times cyanotic. As patients with Raynaud's disease often have extremely moist, as well as cold, extremities, the two conditions seem to shade imperceptibly one into the other. Unlike Raynaud's disease, hyperhidrosis is frequently seen in men, but both diseases are likely to occur in young and emotionally unstable individuals. Dickens[5] must have been acquainted with such a case to have written his classic description of Uriah Heep: "It

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was no fancy of mine about his hands, I observed; for he frequently ground the palms against each other as if to squeeze them dry and warm, besides often wiping them, in a stealthy way, on his pocket handkerchief."

ETIOLOGY

No specific etiologic factor is known for this form of hyperhidrosis, but it is brought about by hyperactivity of the sympathetic nervous system and is exaggerated by nervousness. Just as generalized sweating is frequently seen in high-strung thoroughbred horses in the paddock before a race, in human beings the more localized variety of nervous sweating can be brought out by any difficult mental problem or embarrassing situation. When the normal individual is terrified and breaks out in "a cold sweat," it is the hands and feet that are usually involved. As a result of recent investigations on the role of the premotor cortex and the autonomic centers in the hypothalamus, it is now known that all forms of visceral activity may be influenced by the psychic state of the individual.[6] Cobb,[7] who is making a psychiatric examination of patients with abnormal vasomotor and sudomotor activity, has reached the conclusion that these individuals have a special psychological make-up which, as he puts it, "is characterized by inner emotional turmoil thoroughly covered and repressed beneath a pleasant but formal appearance and superficially co-operative behavior." It is therefore not a far-fetched hypothesis to assume that the cause of these conditions will be found to lie in the corticodiencephalic mechanisms which control our emotional status.

Figure 1. *Photographs of the Hands of a Patient (Case 1) with Hyperhidrosis of Nervous Origin.*

They illustrate the characteristic areas of sweating. Sweat secretion is brought out in black by Minor's[2] starch-iodine method.

TREATMENT

In the treatment of severe hyperhidrosis medical measures have been unsatisfactory. Application of antisudorific preparations, such as 5 per cent formalin, bring about some local reduction in sweating, but at the expense of maceration and irritation of the skin. Radiation of the skin may cause some atrophy of the glands, but it must be pushed to the point of risking a chronic dermatitis. As spontaneous activity of the sweat glands is mediated by the sympathetic nerves, it ceases entirely when these pathways are interrupted. Charts showing the areas of anhidrosis after various operations on the sympathetic nervous system have been published by Roth.[8]

Sympathectomy was first carried out to reduce hyperhidrosis by Kotzareff[9] in 1919. In this operation the resection included only the cervical ganglia, but the excessive sweating appears to have stopped. The anatomical and surgical aspects of this condition were thoroughly explored by Braeucker[10] and by Hesse.[11] The former stated that the sympathetic sudomotor axones to the hand run over the rami communicantes of the two lowest cervical and the first thoracic ganglia. Hesse[11] and his colleague Juzelevskij, however, found that some additional lower fibers leave the second thoracic ganglion, and this has been confirmed by Kuntz.[12] According to Langley[13] and Braeucker,[10] these fibers leave the spinal cord in the motor roots from the fourth to the ninth thoracic segments. Recent observations of Kuntz, Alexander and Furcolo[14] demonstrate that there are higher fibers which emerge over the second and third intercostal nerves, and that a few fibers to the sweat glands in the cat's paw run in the first thoracic root. Clinical experience has shown that sudomotor axones leave the cord as high as in the second and third thoracic roots, but the results

of the operations reported below make it extremely unlikely that any originate above the second thoracic nerve in man. After reaching the paravertebral sympathetic trunk, all these preganglionic axones run upward to the lowest cervical and upper two thoracic ganglia, where they establish synapses with postganglionic neurone cells whose axones are distributed to the cords of the brachial plexus over the gray rami communicantes (Fig. 2).

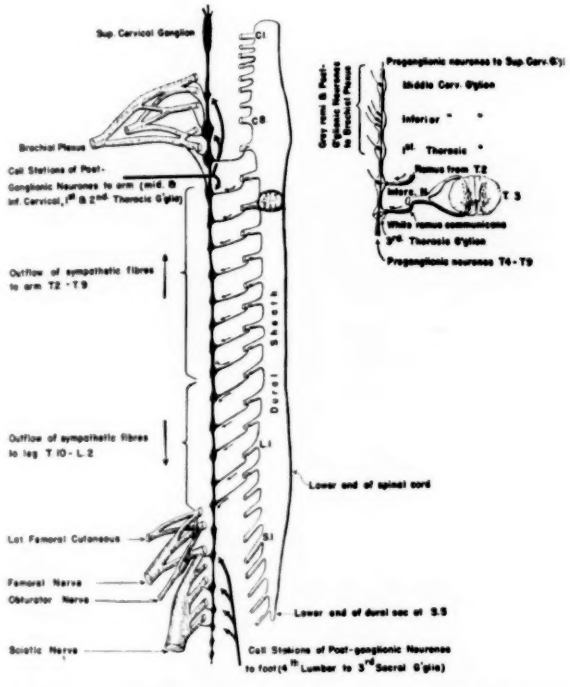
Sup. Cervical Ganglion
C1
C8
Brachial Plexus
Cell Stations of Post-Ganglionic Neurones to arm (mid. & inf. Cervical, 1st & 2nd Thoracic G'glia)
Outflow of sympathetic fibres to arm T2 - T9
Outflow of sympathetic fibres to leg T 10 - L 2
Lat. Femoral Cutaneous
Femoral Nerve
Obturator Nerve
Sciatic Nerve
Dural Sheath
L1
S1
Lower end of spinal cord
Lower end of dural sac at S 2
Cell Stations of Post-ganglionic Neurones to foot (4th Lumbar to 3rd Sacral G'glia)
Grey rami & Post-Ganglionic Neurones to Brachial Plexus
Preganglionic neurones to Sup. Cerv. G'glion
Middle Cerv. G'glion
Inferior "
1st Thoracic "
Ramus from T2
Inferior "
T 3
White ramus communicans
1st Thoracic G'glion
Preganglionic neurones T1 - T9

Figure 2. *The Anatomic Arrangement of the Sympathetic Fibers to the Arm and Leg.*

The nerve supply to the sweat glands of the foot leaves the cord over the lowest thoracic and upper two lumbar nerves, and is distributed to the roots of the sciatic nerve from the fourth lumbar to third sacral ganglion.

Neurosurgical relief of extreme hyperhidrosis of the extremities has been called to the attention of the medical profession through the reports of Braeucker,[10] Pieri,[15] Leriche and Frieh[16] and Roberts,[17] and the more recent article by Adson, Craig and Brown[4] in this country. In the Massachusetts General Hospital the operation was first performed in 1932.[18] Standardized procedures are now available to sever the sympathetic fibers running to the upper and lower extremities. As the vasomotor and pilomotor fibers are mixed with the sudomotor ones, the operation diminishes vasoconstrictor tone, in addition to causing a total paralysis of sweating and of pilomotor activity. In the case of the lower extremities, resection of the second and third lumbar ganglia can be counted on to stop all sweating below the knees, as well as to produce a lasting vasodilatation. In the case of the arm the sympathetic pathway may be interrupted in its postganglionic portion by cervicothoracic ganglionectomy as proposed by Adson.[19] This results in a Horner's sign (drooping of the upper lid, pupillary constriction and enophthalmos), which is somewhat disfiguring, particularly when the operation is done on only one side. Recent investigation[18, 20] has shown that degeneration of the sympathetic fibers leaves some residual vasoconstrictor tone from the direct action of adrenine and sympathin on the arterial walls, which become hypersensitive to these chemical mediators after the nerve fibers have degenerated. It is a well-known physiological fact that this chemical sensitization is more accentuated if the peripheral sympathetic pathway is interrupted in its postganglionic rather than in its preganglionic portion. This action of the sympathomimetic hormones does not affect the sweat glands in any way, as they respond only to the chemical action of acetylcholine,[21] but it is of considerable importance to avoid its action on the vascular tree in persons who already exhibit a tendency to abnormal vasoconstrictor activity. A method of denervation which does not produce a Horner's syndrome and causes only a minimal sensitization of the smooth muscle of the vascular walls has been developed by Smithwick[22] and by Telford.[23] In order to interrupt only preganglionic axones to the upper extremity, the inferior cervical and first and second thoracic ganglia are spared, but the sympathetic chain is cut at the level of its third ganglion and all higher connections with the second and third thoracic roots are severed. The details of these operative methods are beyond the scope of this article, but as success depends on a most exact technic, each step outlined in the original description must be followed with care.

It will be noted in the case histories below that hyperhidrosis in the hands was relieved in 1 case by paravertebral infiltration of alcohol around the first and second thoracic ganglia, with only a single night's hospitalization and without any interruption of the patient's employment. A second equally successful result has been obtained by Freeman.[24] Nevertheless it is my belief that with rare exceptions surgical denervation is the better procedure, as its action is certain and the operative risk is almost nil in this group of young and otherwise healthy individuals. After alcohol block there is considerable risk of incomplete results and some risk of producing a troublesome intercostal neuritis.

Certain precautions should be observed in performing these operations. As stated above, a dis-

figuring Horner's syndrome can be avoided by leaving intact the palpebral and ocular fibers which pass through the first thoracic root, the first thoracic and inferior cervical sympathetic ganglia. When lumbar sympathectomy is performed on a male patient it is essential not to injure the chain above the second lumbar ganglion. If the fibers which run from the upper lumbar chain to the hypogastric plexus are destroyed, loss of the power of ejaculation and sterility will result. Although a sympathetic denervation of the right hand alone may at times suffice, the procedure must usually be carried out bilaterally. Under these circumstances it is safest to do the operation in two stages. The second operation can be done four days to a week after the first, so that the total period of hospitalization is generally under a fortnight when both arms are denervated, and less than three weeks if both lumbar chains are resected.

CASE REPORTS

Case 1. R. T., aged 25. This woman was a stenographer. She had always had excessive perspiration of the palms of her hands and the soles of her feet, which were continually dripping wet. This was so pronounced that drops of perspiration fell from her fingers and made it extremely difficult for her to work as a secretary. This condition became worse when she was excited or nervous, as on meeting strangers. The patient had a normal basal metabolic rate. No other abnormalities were noted except for the fact that her hands were constantly cool, and the skin of her fingers somewhat redder than normal.

On November 23, 1932, a right thoracic ganglionectomy was performed, with resection of the first and second thoracic sympathetic ganglia. Recovery was uneventful. The patient developed a moderate Horner's syndrome. The hand became completely dry after the operation and 10°F. warmer than the left.

The patient was re-examined 4 years later, and still showed the same excessive sweating in her left hand and in both feet. There was a faint but perceptible degree of perspiration in the right palm. She wrote recently that her right hand never sweat and that she was able to work very satisfactorily as a hostess in a hotel.

Case 2. J. C., aged 23. This patient, who at the time he was first seen was a third-year student of medicine, began to notice excessive sweating in the palms and fingers of his hands during the latter part of his high-school years. This had become progressively worse through his medical-school career. It had become embarrassing to do physical examinations on patients, and when he assisted at operations his rubber gloves would fill with sweat. When he was free from all emotional strain the condition might clear up entirely. He had tried formalin soaks, radiation of the skin and psychotherapy without benefit. Physical examination showed a healthy young adult without any abnormalities except the unusual sweating. His hands were at times distinctly colder than normal, but at other times were quite warm. As he could not afford the time needed for the usual sympathectomy, I discussed with him the possibility of blocking the sudomotor fibers by paravertebral alcohol injection. This was finally decided on, with the understanding that the nerves leading to one hand should be blocked, and a year allowed to intervene before deciding whether to employ alcohol injection or surgery on the other extremity.

On October 6, 1933, alcohol was injected paravertebrally around the upper three thoracic sympathetic rami and ganglia on the left side, 4 cc. of 95 per cent alcohol at each level.* This resulted in a striking Horner's sign and a hot, dry hand. The patient resumed his classwork the next morning and noticed no disagreeable effects except a barely perceptible hyperesthesia along the distribution of the upper intercostal nerves, which lasted about 1 month. The left hand remained completely dry for 6 months, and then showed the slightest possible trace of moisture (Fig. 3). The Horner's sign had gradually disappeared. At the end of 1 year the patient returned for injection on the opposite side.

Figure 3. *Photographs of the Hands of a Patient (Case 2) One Year after Paravertebral Alcohol Injection on the Left Side.* (Reproduced from *The Autonomic Nervous System: Anatomy, physiology, and surgical treatment* [New York: 1935] by courtesy of the publisher, The Macmillan Co.)

There is extreme sweating on the right, but only traces of moisture on the left.

On November 30, 1934, a paravertebral alcohol injection was made on the right side. Again the injection caused no inconvenience, and the patient returned to his classes the following morning. No Horner's sign was produced on this side, although the sympathetic denervation of the arm appeared to be complete.

Almost 5 years have now intervened since the injection was done on the left side. The hands continue to be free from any excessive moisture. However, the patient states that in extremely hot weather his hands perspire about as much as those of a normal individual. This indicates that there has been a partial regeneration of the sudomotor fibers.

*The technic of paravertebral injections is described elsewhere.[35]

Case 3. L. L., aged 23. This patient, also a medical student, had noticed excessive sweating of the hands and feet for 13 years. This had recently increased to an incapacitating degree. Treatment with formalin and x-ray had been ineffective. Otherwise he had always been in excellent health. He showed marked sweating of the hands, with a sharp line of demarkation at the wrists. Beads of moisture stood out on his palms and the soles of his feet and frequently dropped off. The extremities were cold as well as wet to the touch. The patient admitted that he had been "nervous" as long as he could remember.

On August 21, 1936, a right preganglionic sympathectomy was performed. Sweating tests performed on discharge showed no trace of perspiration above the second rib on the right side. The patient returned to medical school 1 month later and had no further trouble with perspiration in his right hand (Fig. 4). Nine months later

Figure 4. *Photograph of the Hands of a Patient (Case 3) Nine Months after Right Thoracic Sympathectomy.*

The right palm remains completely dry, the left is dripping wet.

he returned for operation on the left side. After each operation he made a smooth and uneventful convalescence.

A follow-up letter 3 months after the second operation stated that the left hand had remained completely dry and warm. The right hand showed a trace of perspiration along the medial side of the palm. This was too slight to be of any concern, and the remaining area of the right arm, and all the left arm, as well as the head and neck, remained completely dry. The patient was in excellent condition and felt better both mentally and physically.

Case 4. C. J., aged 29. The patient, who did secretarial work, stated that his palms and soles had been cold and clammy for 15 years. At times of nervous strain they actually dripped sweat, so that the condition became a social as well as an economic handicap. No other part of his body sweat to an abnormal degree.

On September 10, 1936, a right preganglionic sympathectomy was performed. One week later, the patient after being heated in a chamber at 130°F. broke out in a generalized perspiration. The right hand showed no moisture, and the right side of his face, neck and upper chest remained strikingly dry, in contrast to the left side, which was covered with large beads of perspiration. On September 19, 1936, a similar operation was performed on the left side.

Three months after the second operation the patient reported that he was back at work and was cured. Six months later he was seen in New York by a physician, who reported that the hands remained dry, warm and pink.

Case 5. J. R., aged 32. This patient, who had just finished medical school, was about to start on a surgical internship. He was a well-built, athletic individual, but with dripping wet palms and fingers, which made surgical work nearly impossible. In addition to hyperhidrosis he showed a moderate degree of increased vasoconstrictor tone in the extremities. A physical examination showed no other abnormality.

On June 7, 1937, a right preganglionic sympathectomy was done. The patient showed a transitory tendency to perspire in the denervated area about the 4th day after operation. We have observed this on a number of occasions after preganglionic sympathectomy, and have ascribed it to a transitory stimulation of the degenerating preganglionic fibers. It has never lasted over 1 day.

Six months later the patient wrote in answer to a questionnaire that his hand remained practically free from moisture. He had noticed no disagreeable sequelae, and the hand had remained pleasantly warm all the time. He was delighted with the results of the operation.

Case 6. A. McD., aged 36. This patient, a lawyer, well-built but somewhat apprehensive, had noticed excessive sweating of his hands and feet for many years. At first he minded it most in his feet, as his socks were always dripping wet, but at the time of entry his hands were even worse and bothered him extremely in his courtroom work. As I observed him he was constantly wiping his hands with his handkerchief. Except in extremely hot weather, sweating was confined entirely to the characteristic areas. The skin over the hands and feet was corrugated as though the extremities had been soaked in hot water. There had been no visible vasospasm. The general condition was good, and the patient had always been in excellent health. He had tried formalin soaks and found that these helped somewhat with his feet, but very little with his hands. His basal metabolic rate was within normal limits.

On August 31, 1937, a right preganglionic sympathectomy was performed. Since that time his right hand has remained completely dry. Nine months later he returned requesting operation to relieve the extreme sweating of his feet. In spite of frequent formalin soaks he had not been able to reduce the sweating to the point where it would not soak through his shoes. The skin over the palmar areas and toes was severely macerated. On June 2, 1938, a resection of the right lumbar sympathetic chain with the second and third ganglia was done by Dr. Reginald H. Smithwick. On June 9, 1938, a left lumbar sympathectomy was performed. The patient made a very smooth convalescence from both operations and was ready to go home 18 days after the first operation.

In a follow-up examination, September 12, 1938, no signs of moisture could be detected in either foot or in the right hand. The patient was most grateful.

SUMMARY AND CONCLUSIONS

Excessive sweating of the palmar surfaces and fingers and of the soles and toes is a not uncommon condition in nervous young people. The wetness may become so extreme as to be incapacitating, especially in certain vocations which require skilled work with the hands.

Medical measures of control are unsatisfactory in the more severe cases.

Sympathetic denervation of the arm and leg offers a safe and certain cure. The operation results in warm and dry extremities. If care is taken to avoid the ocular fibers (the section of which results in Horner's syndrome) and to leave the highest portion of the lumbar chain in the male intact (in order to preserve the power of ejaculation), there are no annoying sequelae.

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Discussion

Dr. Donald Munro, Boston: There are two things I should like to emphasize. In the first place, I doubt if there is another as skillful a surgeon of the sympathetic nervous system working today as Dr. White, and his description of this operation, which looks and reads so simply, should not be allowed to lead us astray and into thinking that we can do one before breakfast, as it were, because it is not an easy operation to do. Secondly, we should all realize that we have listened to a presentation which we can accept at its absolute face value, and concerning which discussion is unnecessary.

Dr. John Homans, Boston: I should like to ask Dr. White whether there is any such thing as excessive sweating without at the same time some evidence of vasomotor spasm. Also, in making a diagnosis is it necessary to be sure that one can secure full vasodilatation by a novocain block or in some other way, before using this operation to prevent sweating?

Dr. William J. Mixter, Boston: I have watched Dr. White's cases with the greatest interest. The results are little short of marvelous. No one would do this operation for a person who sweats only moderately. There are not very many of these bad cases, but those patients who really sweat profusely are perfectly wretched. They will go to almost any length to get relief. Here is an operation which gives them positive relief with very little risk, an operation which has to be done with a good deal of care, and at the same time one which in proper hands carries a very low mortality.

Dr. White (closing): To answer Dr. Homans's first question: most of these patients had cold as well as moist hands, but at least one had hands as warm as those of a normal individual. So far as testing with novocain goes, I think the anatomical arrangement of the sweat fibers is so constant that, if you are doing the operation merely to stop the sweating, there is no need to do a novocain block. We did it in our early cases but we have not used it since then. However, if it is a case of cold as well as sweaty hands, and particularly if there is any sclerodermatous change, it is best to test and see how much vasodilatation can be obtained by paralyzing the vasoconstrictor nerves.

TULAREMIA

Report of a Case of the Typhoidal Form

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TULAREMIA is almost unknown in New England, and the rarity of its appearance here is not wholly explained. Francis[1] shows that up to 1937 only 4 cases had been reported from the New England States. In 1929 in North Scituate, Rhode Island, a man contracted tularemia after tearing apart three rabbits found dead on his farm. In 1929 in Massachusetts a man contracted the disease after dressing a cold-storage rabbit obtained from the Boston market. In 1931 in Claremont, New Hampshire, a person became ill after dressing two rabbits killed near-by. A fourth case occurred in 1933 in the Moosehead Lake region of Maine, where a hunter contracted the disease after skinning a red fox. No case has ever been found in Vermont or Connecticut, and none have been reported from anywhere in New England since 1933. An editorial[2] in this *Journal* in 1937 commented on this region's freedom from tularemia, and warned against the importation of Western rabbits to augment our own stock.

The case of tularemia here described is the second ever reported in this state and the first in the Cape Cod region. Its appearance there is felt to be significant, for this is a tick-infested region where, given rabbits infected with tularemia, the more widespread transmission of the disease might easily become established.

CASE REPORT

The patient, a 10-year-old girl, was first seen in her home in West Falmouth on July 3, 1937, because of fever of unknown cause of 1 week's duration. Seven days before she had had a chill lasting 1 hour. This was followed by a temperature of 102°F., which rose to 103.5°F. during the day. There was a slight headache, some constipation and rather more gas in the bowels than usual. Aside from these minor complaints the patient felt well. Prior to June 27 she had been perfectly well in all respects.

The recent past history presented no known contact with infectious disease, no illness during a trip to the Orient, from which she had returned a month previously, no significant association with tuberculosis, no consumption of raw milk at any time and no bites by insects or ticks. In her parents' minds the only incident of importance was that the child's Springer spaniel puppy had been quite ill with fever and cough for 3 days before the onset of her illness. This fact, however, was regarded by her physicians as unimportant and was neglected until later.

The first week of illness was characterized only by the persistence of fever from 101 to 104°F., without malaise. The patient felt well enough to go out and play as usual. The past history was irrelevant.

Physical examination, on July 3, 1 week after onset, revealed nothing of significance except a possibly enlarged spleen. The skin and mucous membrane were clear and without eruptions. The tonsils were large but without evidence of infection. No enlarged lymph nodes could be felt. The heart and lungs were clear. The pulse rate was 99, and the blood pressure 108/68. The extremities and reflexes were normal. There was no stiffness of neck or back. A Kernig test was negative. The urine had been normal on a previous examination, and the white-cell count was 6000.

At the first visit the high fever, relatively slow pulse, low white-cell count and probable enlargement of the spleen led to a tentative diagnosis of typhoid or paratyphoid fever. Subsequent laboratory studies failed to substantiate this diagnosis. The Widal test, questionably positive at first, was later three times negative.

On July 12, because the fever continued to range from 101 to 103.5°F., the patient was transferred to the Massachusetts General Hospital for study. Persistently high fever to 103°F. and a brisk nosebleed were the sole significant clinical observations during her 4-day hospital stay. She was seen by two consultants, who found her physical examination essentially normal. At no time were skin lesions seen. No lymph nodes were enlarged. The spleen was never thought to be enlarged after the first examination. There were no localizing signs of any sort. The patient was never prostrated and retained a remarkable sense of well-being.

On July 16 she was sent home after completion of studies, undiagnosed. Her fever fell by lysis and permanently reached normal September 1, 9 weeks and 3 days after its abrupt onset. Blood collected on the day of discharge was sent to the National Institute of Health in Washington, District of Columbia, to be tested for typhoid fever, undulant fever and tularemia. The blood was reported positive for tularemia in a titer of 1:1280. It was negative for typhoid and undulant fevers.

The white-cell count on June 30 was 6000 and on July 3 had risen to 17,000. On July 12 the hemoglobin was 80 per cent and the red-cell count was 4,530,000; the white-cell count had fallen to 11,400, with 74 per cent polymorphonuclears, 20 per cent lymphocytes, and 6 per cent mononuclears. There was moderate achromia. The corrected sedimentation rate was 0.7 mm. per minute and the hematocrit 37.7 per cent. A blood culture taken July 12 showed no growth after incubation for 12 days. A catheter specimen of urine showed no growth. Daily urine specimens were negative except for a few red blood cells on one occasion. Stool examination on July 13 showed no pathogenic organisms. No parasites or amebae were seen on warm-stool examination. A throat culture on July 12 showed no hemolytic streptococci. An electrocardiogram on July 12 was within normal limits, and an x-ray film of the chest taken the next day showed the lung fields to be clear. The heart, mediastinum and diaphragms were not remarkable.

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Typhoid agglutination was partially positive on a specimen taken July 3 but negative on July 6 and 12 and October 9. Tests for paratyphoid fever were negative on four occasions. Blood taken for undulant fever was negative on July 3. Blood drawn July 16 was negative for undulant fever but positive for tularemia in a titer of 1:1280. Agglutination tests on October 9 were negative for undulant fever, negative for the Weil-Felix reaction and positive for tularemia in a titer of 1:1280.

The tuberculin test was negative to 1 mg. of old tuberculin. A blood Wassermann test was negative. A skin test done on October 9 for tularemia, with a suspension of killed *Pasteurella tularensis* provided by Dr. Lee Foshay, was strongly positive.

It was due solely to the fact that the child's parents referred again and again to her sick dog that the tularemia agglutination was done at all. A young Springer spaniel puppy, which had been in the Middle West during its early months, had been given to the patient a month before the onset of her illness. The dog had been well until three days before the patient fell ill. At that time it became sickly and feverish and coughed, recovering in three days. Since it was an affectionate puppy its contact with the patient was constant and close. She had, however, received no bites or scratches from the dog; or tick or flea bites at any time before her illness. Following the diagnosis of tularemia, blood was collected from the dog on August 4, five weeks after its illness, and was found positive for tularemia in a dilution of 1:40. The source of the dog's infection was not found, but may have been a tick bite or the eating of a rabbit which had died of tularemia.

This is the only case on record where definite relation between the disease in a dog and a human being has been shown. Experimentally tularemia has been produced in dogs, and Francis[1] reports 1 case following a dog bite, but the dog was never shown to have had the disease. Puppies are more easily infected than adult dogs. Although a titer of 1:40 is one of low dilution, it may not go higher than this in human beings known to have had tularemia.[1] The appearance of a positive agglutination in both child and dog in the case reported would seem to be more than coincidence. Infection of the child was probably by the dog's saliva from hand to mouth.

IMPORTATION OF WESTERN RABBITS TO CAPE COD

In 1936 the Division of Fisheries and Game of the Massachusetts Department of Conservation[3] authorized the importation into this state of cottontail rabbits from the West. The director of the division, it was announced, had conferred with officials of the New York Conservation Department, which had for a number of years been importing cottontails from the West, and it had been planned to make the Massachusetts system of importation conform as closely as possible to that employed in New York. Plans were being formulated, it was stated, for the importation of a considerable number of cottontail rabbits during 1937.

Table 1. *Cottontail Rabbits Released by the Division of Fisheries and Game.*

TOWN	NO. OF RABBITS	DATE
Harwich	5	March 31, 1937
Truro	9	March 31, 1937
Wellfleet	5	March 31, 1937
Falmouth	8	March 31, 1937
Barnstable	6	March 31, 1937
Total	33	

During the spring of 1937, western cottontail and jack rabbits were released on Cape Cod, the former by conservation officers and the latter by local sportsmen's clubs, as shown in Tables 1 and 2.*

J. Arthur Kitson, in charge of propagation in Massachusetts, stated in a letter dated December 8, 1937, that all rabbits received dead were examined by a competent pathologist and that no tularemia was found. But in none of these examinations were guinea pigs inoculated with tissue.

Table 2. *Jack Rabbits Released by Sportsmen's Clubs.*

TOWN	NO. OF RABBITS	DATE
Harwich	12	Middle of May, 1937
Provincetown	16	May 24, 1937
Barnstable	14	June 21, 1937
Truro	12	March 24, 1937
Wellfleet	12	May 4, 1937
Dennis	24	Latter part of May, 1937
Total	90	

(For the guidance of those especially unfamiliar with tularemia, the disease is altogether too easily overlooked in the gross. Guinea-pig inoculation has been shown to be the only sure method of diagnosis and identification.)

With these facts in mind, it seems particularly significant that this young child, with no known source of infection or trauma or bites, developed tularemia in a region where the disease had never been seen. It is also significant that the common wood tick, *Dermacentor variabilis,* is prevalent on Cape Cod, and that these ticks, feeding chiefly on small rodents during the larval and nymphal stages, feed indiscriminately on both men and animals during the adult stage. Thus the danger of tick-born tularemia is constant in this region.

It is noteworthy that three months after the release of Western cottontail rabbits in the Falmouth district this isolated case of tularemia ap-

*Information supplied by J. Arthur Kitson.

peared in the town of Falmouth. It appears probable that the child's dog killed or ate one of these imported rabbits with tularemia, or was bitten by an infected tick. In view of the evidence presented, it seems logical to suppose that the puppy's illness was tularemia. The transmission to the child was apparently direct, since no other source could be found.

HISTORICAL BACKGROUND

Tularemia as we know it was originally confused with bubonic plague, both clinically and bacteriologically. Wherry[4] in 1908, when he was bacteriologist of the San Francisco Board of Health, published an excellent review of this problem. His account may be briefly summarized as follows:

In 1903, three years after the first appearance of bubonic plague in this country in San Francisco, Assistant Surgeon Rupert Blue, United States officer in charge of plague suppression, suspected that ground squirrels, which were dying in large numbers, were afflicted with the same disease as were human beings, and were responsible for its conveyance to them in the widely scattered areas from which it was being reported. That the squirrels had a plague-like disease was clear, but that they transmitted it directly to human beings was not proved. Soon, however, a boy of ten in Los Angeles was bitten on the finger by a sick ground squirrel which he picked up near his home. Four days later he became ill with a plague-like disease, thought to be bubonic plague. From the suppurating glands of this boy, an organism like the bacillus of plague was cultured. As a result, until 1909 squirrel plague (now known as tularemia) and human plague were thought to be the same disease. In 1910, however, Post-Assistant Surgeon George W. McCoy,[5] of San Francisco, published a paper showing that there was a distinct difference between bubonic plague and squirrel plague, and that although the pathological and bacteriological findings were similar, they were not identical.

In 1911 McCoy and Chapin[6] identified the organism of squirrel plague, cultured it, transmitted it to guinea pigs and named it *Bacterium tularense* (*Pasturella tularensis*), after Tulare County, California, where the disease was first observed.

In 1914 Wherry and Lamb[7] reported the first case of human infection with the organism discovered by McCoy and Chapin. This was a case of ulcerative conjunctivitis with lymphadenitis from which organisms identical with *Past. tularensis* were recovered. Since 1914 tularemia has been shown to be widespread throughout the United States, with the exception of New England.

CLINICAL TYPES

The literature is filled with clinical, pathological and bacteriological studies of tularemia, but Francis[8–10] has probably contributed most to the early clarification of the disease in its various aspects. He describes four clinical types, as follows. *Ulceroglandular:* The primary lesion at the site of inoculation is a papule of the skin. This papule later ulcerates and is accompanied by enlargement and often ulceration of the regional lymph nodes. *Oculoglandular:* The primary lesion is in the eye (transmitted from the hands) and is accompanied by enlargement of the regional lymph nodes. *Glandular:* No primary lesion is found at the site of inoculation, but there is fever, and infected regional nodes are found. Often there is a generalized adenopathy. *Typhoidal:* Persistent fever is the outstanding feature. There is no primary ulceration and no detectable lymph-node enlargement.

It is with the typhoidal type that we are particularly interested. This type is so named because of its similarity to typhoid fever, with which it is often confused. At other times it passes for fever of unknown origin, septic infection and influenza. The pulmonary lesions in the typhoidal form have led to the diagnosis of tuberculosis or of pneumonia. The cross-agglutinations with *Brucella abortus* and *Br. melitensis* have caused it to be called undulant fever. A clinical diagnosis of typhoidal tularemia is rarely possible. Where persistent, unexplained fever exists, however, specific agglutination tests offer the only clue to diagnosis.

The onset of typhoidal tularemia is abrupt and without warning, and is marked by chills, fever, headache, vomiting, sweating, prostration or joint pains. There is an initial rise of temperature, followed by remission of the fever and symptoms for two or three days, then a return of the fever, which is constantly elevated or spiking, for from three to ten weeks, disappearing by lysis.

It is of interest that patients may retain a sense of well-being throughout the course of a typhoidal tularemia of several weeks' duration with persistent fever; however, prostration is usual. Nosebleeds during the second and third weeks are not uncommon. Headache may be severe or lacking. The white-cell count is usually low in the early stages, later rising as high as 16,000. Foshay[11] has shown in a series of 400 unselected cases of acute tularemia that the typhoidal type is a generalized infection from the start, with minor cutaneous or regional lymphatic involvement, or more commonly none at all. In the other three types of the disease the lymphatic system appears to bear the brunt of the attack. Multiple lesions in the deep

organs and lungs characterize the typhoidal type.

The mortality rate of the typhoidal type of tularemia Foshay found to be approximately 40 per cent, nearly four times that of other clinical types, and the incidence of complicating pneumonia four times the average in the other three types.

Septicemia, Foshay showed, occurred in 1 out of every 17 cases without forewarning. The chief clinical signs of septicemia are progressive enlargement of the liver and spleen, sometimes with increasing jaundice and septic fever. Hyperpnea and cyanosis, meningeal and cerebral involvement, diarrhea, progressive bronchopneumonia, acute renal involvement, pleurisy, pericarditis and peritonitis may appear. Septicemia is the chief cause of death attributable to tularemia alone, but pneumonic lesions were shown to be present in half of Foshay's fatal cases.

SOURCES OF HUMAN INFECTION

Human beings become infected with *Past. tularensis* by contact with the raw flesh or blood of infected animals, by the bites of blood-sucking insects and flies and by the eating of insufficiently cooked infected meat. Francis[1] in a recent report pointed out that twenty varieties of wild life contract and transmit tularemia. The cottontail rabbit, the snowshoe hare and the jack rabbit account for 90 per cent of all human infections.

Most infections occur through wounds or abrasions in the skin, most frequently of the hands, but *Past. tularensis* can penetrate the unbroken skin. Wood ticks, dog ticks, horseflies, houseflies, fleas and bedbugs have been shown to cause infection. Tree squirrels and opossums have been responsible for cases of tularemia. One case each has been reported from skinning a sage hen, coyote, deer, red fox and bull snake. Two cases each came from contact with quail, ground hog and skunk. Two patients had been scratched by cats. Single cases have followed from the bites of the cat, skunk, coyote, tree squirrel, opossum, hog, lamb, white rat and dog. Contamination in the latter group of cases is believed by Francis to be from the animals' mouths. Market men, hunters and meat dressers are most frequently affected, usually with the ulcerative type. Laboratory workers have frequently been infected, with a high incidence of the typhoidal type of the disease.

NON-CONTAGIOUSNESS AND IMMUNITY

According to Francis[1] there is no record of transfer of infection from man to man. Doctors, nurses and others attendant on the sick have not contracted the disease. One attack confers a lasting immunity. Blackford,[12] however, reports 2 cases of ulcerative dermatitis where living organisms were obtained five to twenty-one months after the initial infection. Foshay, discussing Blackford's paper, says that relapses are not frequent but may be seen weeks or months after the initial infection. These relapses, he believes, are due to residual living bacteria in the tissues and most commonly occur in cases with ulcerating skin lesions and chronically suppurating lymph nodes.

AGGLUTINATION TESTS

Francis[8] states that there is apparently a complete absence of agglutinins for *Past. tularensis* during the first week of the disease. The appearance of specific agglutinins occurs sometime in the second week, with an abrupt rise in titer in the third week, reaching its maximum in the fourth to seventh week. After the eighth week the titer usually falls, but positive agglutinins have been known to remain as long as twenty years.

Serums from cases of tularemia may show agglutinations with *Br. abortus* and *Br. melitensis*. Francis[8] reports that of 579 such serums 129 showed agglutination with *Br. abortus* and *Br. melitensis,* while 441 failed to cross-agglutinate. Many serums showing no cross-agglutination had the highest titers (1:1280 to 1:2560) against *Past. tularensis*. Serums from tularemia patients agglutinate *Past. tularensis* in much higher titer and much more quickly than they do *Br. abortus* or *Br. melitensis*. Serums from cases of undulant fever may show cross-agglutination with *Past. tularensis*. Of 93 such serums, 31 showed some degree of cross-agglutination.

Foshay[19] recognizes cross-agglutination reactions between tularemic serums and those from cases of Rocky Mountain spotted fever. He finds that tularemic animal serums invariably show a positive Weil-Felix reaction, but those of human subjects rarely do. He has recorded only 4 cases in which human serums have given such a reaction.

SKIN TESTS

Foshay[13] has shown that an intradermal test done with a detoxified bacterial suspension of *B. tularensis* is the earliest diagnostic aid for determining the presence of tularemia. The allergic skin response is specific and reliable. Positive reactions occur as early as the fourth day of illness, almost a week before agglutinins appear in the blood. He has demonstrated that positive skin reactions are constant in the presence of tularemia, but do not occur in normal persons or in the presence of other acute infections.

SPECIFIC THERAPY

Symptomatic treatment of tularemia still holds the place it should in any acute infection, but specific serum now offers the safest and surest method of treatment. Intravenous chemotherapy with arsenicals[14] and iodides has proved of no value. X-ray therapy[15] for primary local lesions has been thought to shorten the course of the disease if applied in the first four days of the disease, but is of doubtful value. Immunotransfusions have been shown of value, but suitable donors are difficult to find. Foshay[19] reports a case of acute tularemia treated as effectively by immune serum as by antiserum.

The antiserum developed by Foshay[16–18] is of specific therapeutic value. There is, with its use, a definite antitoxic action, with a fall in temperature, disappearance of symptoms and regression of lymph nodes, if present, and healing of primary lesions. The usual dose is 30 cc. intravenously for adults, although an additional 15 cc. may be given if improvement fails to appear. Severe cases with complications may receive up to 60 or 70 cc. Serum reactions may follow the administration. Goat serums[16] have proved effective in the past. Surgery should be used only for the incision of acute suppurating glands.

PROPHYLAXIS

The prevalence of the disease among wild rabbits makes its eradication impossible, but those who handle or dress them should protect themselves with rubber gloves and frequent, careful washing of the hands. Possibly hunters and market men who handle rabbits from grossly infested areas should be immunized. Foshay urges this for those doing laboratory work or animal experimentation, feeling that it is the only prophylactic measure of value.

SUMMARY

A case of tularemia contracted in Falmouth, Massachusetts, is reported in a girl of ten. It is the second case ever reported in Massachusetts and the fifth in New England.

No known source for this infection could be found except the child's young Springer spaniel puppy. The dog was ill three days before the abrupt onset of the infection in the child, and its blood serum later agglutinated *Past. tularensis,* as did the child's.

Three months preceding the appearance of this case Western cottontail and jack rabbits were shipped to Cape Cod. Eight of these rabbits were released in the vicinity of Falmouth.

The conclusion seems justified that the dog killed or ate a Western rabbit that had tularemia, became ill himself and transmitted the disease to the child.

If tularemia has become established on tick-infested Cape Cod, such a condition of affairs is of extreme public-health importance.

A brief review of the historical and clinical aspects of tularemia is presented.

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NEOPLASMS OF THE TESTIS*

A Study of the Results of Orchidectomy, With and Without Irradiation

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THIS paper originated as the result of the return to the Mayo Clinic, for other causes, of several patients who had been operated on for highly malignant tumors of the testis and who appeared to have survived longer than was considered quite reasonable. Now it is very difficult and probably impossible to determine the accepted standard opinion as to the expectancy of life for victims of this malady. The literature lends but feeble assistance to such endeavors, since the reports are made in such form as to be quite difficult of comparison. Commonly a certain percentage of patients are stated to have survived operation or irradiation or both but without clear indication of the duration of survival. Again, an array of figures is presented on patients said to have had a tumor of the testis, but it is not clear what the word "tumor" is intended to convey. However, we think it may safely be suggested that average expert opinion holds that practically all tumors of the testis are malignant; that the malignancy of most of them is of relatively high grade, with the exception of the adult teratoma; that the disease is very fatal and that survival beyond five years is uncommon; that irradiation in competent hands has materially extended the life expectancy, with or without orchidectomy; and that the relatively recent discovery of the presence of anterior pituitary-like substances in the urine is of both diagnostic and prognostic importance.

We shall be able to submit statistical data showing the ultimate result in a relatively large number of cases. Particular attention is here called to the fact that in the series analyzed in this study for survival and to be presently referred to, 98 per cent of the patients were followed for at least five years. Unfortunately we shall not be able to offer any evidence on the value, either in diagnosis or prognosis, of the discovery of anterior pituitary-like substances in the urine. Our experience with this method is still confined to a group of cases too small to warrant any definite conclusions.

This study is based on an analysis of 363 cases seen at the Mayo Clinic between January 1, 1910, and January 1, 1937. The mean age of these patients was 36.2 years, the youngest being seventeen months and the oldest eighty-four years. It is commonly stated that in something like 80 per cent of cases the disease occurs between the twentieth and fortieth years. Our figures tend to show a somewhat higher range. Sixty-two per cent of the patients were between the ages of twenty and forty, and 20.9 per cent between forty and fifty. This is a somewhat higher figure than is commonly given.

Of the 363 patients, 148 were seen in the first instance at the Mayo Clinic; 215 came to the clinic only after they had been treated or a diagnosis had been made elsewhere, and they were sent primarily for irradiation, many of them having very extensive metastases. Of the 148 first seen at the clinic, 142 were treated by orchidectomy, with or without irradiation. Of the 215 other patients, all were treated at the clinic by irradiation, and 165 of them had had operation elsewhere. This distribution is shown in Table 1.

Table 1. *Summary of Treatment in All Cases, with a Listing of the Tissue Available for Re-examination.*

Treatment	No. of Cases		Tissue Available for Histological Re-examination	
			Testicular	Metastatic
Orchidectomy		142		
With irradiation	105		101	0
Without irradiation	37		36	0
Other operation		6		
Exploration	3		0	0
Biopsy only	3		1	0
Irradiation only at clinic		215		
With previous operation elsewhere*	165		18	6
Without previous operation elsewhere†	50		0	6
Totals		363	156	12

*For example, orchidectomy, exploration.
†Except possibly biopsy.

Analysis of Cases Treated by Orchidectomy with or without Irradiation

Since the evidence in regard to patients coming to the clinic after operation elsewhere was necessarily incomplete, we have thought that the purposes of this paper would be best served by a careful analysis of the 142 cases in which orchidectomy was performed at the clinic and in which all the pathological examinations were made there.

*Read before the meeting of the American Medical Association, San Francisco, June 13–17, 1938.

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Table 2 shows the pathological diagnoses made on a recent check of the specimens.* The most striking point to be observed is the relatively high percentage of neoplasms classified as seminoma (59.2 per cent). It should be stated here that we regard seminoma as a variety of carcinoma, and are still neutral in our opinion as to whether it is a separate entity, a view long championed by Chevassu but not yet finally determined. It is not impossible that with the accumulation of evidence in regard to the presence and quantity of anterior pituitary-like hormonal substances in the urine, the question of the origin of this tumor may be finally determined. The other point clearly brought out by this table is the high grade of malignancy of the group classified as seminoma when malignancy is rated by the examination of the histologic specimen. It will be noted that all 84 of these cases are classified as Grade 4. This is in some, though not very striking, contrast to those classified as adenocarcinoma or adenocarcinoma with teratoma.

Table 2. *Pathological Findings in the 142 Selected Cases.*

Histological Diagnosis	No. of Cases	Per Cent	Rating of Malignancy				
			Grade 1	Grade 2	Grade 3	Grade 4	Not stated
Adenocarcinoma*	28	19.7	0	4	9	12	3
Adenocarcinoma with teratoma	21	14.8	1	2	13	5	0
Seminoma	84	59.2	0	0	0	84	0
Miscellaneous†	9	6.3	0	0	0	0	9
Total	142	100	1	6	22	101	12

*Two cases not recently reviewed.
†Teratoma, 4; embryoma, 3; sarcoma, 1; no histological diagnosis, 1. Three cases were not recently reviewed.

Three-, Five- and Ten-Year Survivals

These figures, according to type of lesion and irradiation, are presented in Table 3. It is at once evident that the survival rate of patients having so-called seminoma is very much higher throughout all these periods than that of patients having tumors classified as carcinoma, irrespective of the use of irradiation. Among the patients with carcinoma, there appears to be a higher survival rate for the three- and five-year periods in those treated by orchidectomy without irradiation than in those treated by orchidectomy with irradiation. These figures, however, are somewhat misleading, since the number of patients not treated with irradiation is relatively small and hence, statistically, relatively unreliable. Moreover, the group of patients given irradiation contained a much larger per-

Table 3. *Three-, Five- and Ten-Year Survivals.*

Classification	Patients Treated*	Patients Traced	Lived Three or More Years		Patients Treated*	Patients Traced	Lived Five or More Years		Patients Treated*	Patients Traced	Lived Ten or More Years	
			No.	Per cent of those traced			No.	Per cent of those traced			No.	Per cent of those traced
According to Type of Lesion and Irradiation												
Carcinoma†												
All cases	43	43	14	32.6	41	41	12	29.3	31	30	8	26.7
Without irradiation	12	12	5	41.7	12	12	5	41.7	12	11	3	27.3
With irradiation	31	31	9	29.0	29	29	7	24.1	19	19	5	26.3
Seminoma												
All cases	71	69	53	76.8	64	62	42	67.7	41	38	18	47.4
Without irradiation	21	19	13	68.4	19	17	10	58.8	18	15	7	46.7
With irradiation	50	50	40	80.0	45	45	32	71.1	23	23	11	47.9
According to Type of Lesion and Metastasis												
Carcinoma†												
Without metastasis	29	29	12	41.4	27	27	10	37.0	21	20	7	35.0
With metastasis	14	14	2	14.3	14	14	2	14.3	10	10	1	10.0
Seminoma												
Without metastasis	55	54	45	83.3	49	48	36	75.0	32	30	15	50.0
With metastasis	16	15	8	53.3	15	14	6	42.9	9	8	3	37.5
According to Type and Duration of Lesion												
Carcinoma†												
Duration less than 1 year	31	31	11	35.5	30	30	10	33.3	24	23	7	30.4
Duration 1 year or more	10	10	3	30.0	9	9	2	22.2	5	5	1	20.0
Seminoma												
Duration has been 6 months	14	14	8	57.1	14	14	8	57.1	8	8	3	37.5
Duration 6 months - 1 year	16	15	12	80.0	13	12	8	66.6	9	8	4	50.0
Duration 1 year or more	31	30	25	83.3	27	26	18	69.2	16	14	7	50.0

*Inquiry as of January 1, 1937. The three-year group comprises the patients treated three or more years prior to the time of inquiry, that is, 1933 or earlier; the five-year group comprises those treated in 1931 or earlier; the ten-year group comprises those treated in 1926 or earlier.
†Includes carcinoma with teratoma.

*Except in 5 cases in which tissue was no longer available for examination.

centage of those with metastases (42 per cent) than did the group without irradiation (8 per cent). It is interesting to note that at the end of ten years there is no substantial evidence that the survival rate has been affected by irradiation.

Turning now to the patients with seminoma treated by orchidectomy, there is a substantial difference, favorable to the group that had irradiation, in the survival rates for the three- and five-year periods. On the other hand, there is no clear evidence that the survival rate at the end of the ten-year period has been significantly influenced by irradiation. The more favorable three- and five-year rates for the group that had irradiation is the more impressive when we note the facts with respect to metastases. This group had a somewhat larger percentage of known metastases (26 per cent) than the patients treated by orchidectomy without irradiation (15 per cent). Thus the evidence in favor of the value of irradiation for patients with this lesion seems substantial, and it is a fair conclusion that the survival rate for the three- and five-year periods is improved by this treatment.

The situation according to type of lesion and the known presence or assumed absence of metastases is also shown in Table 3. It should, of course, be understood that many of the patients in whom metastasis was not noted may be assumed to have had some extension of the disease to the lymph nodes, which were nevertheless not sufficiently enlarged to be palpable. In fact, the diagnosis of metastasis by physical examination, except where the growth is massive, is notoriously uncertain. On the other hand, Table 3 clearly shows that the prognosis at all three periods is distinctly better for patients in whom metastasis is not known to be present. Perhaps the most outstanding fact here shown is the extraordinarily high survival rate (75 per cent) of patients with seminoma but without known metastasis over the five-year period. Again, the finding of a lower survival rate for the groups with known metastasis is made more striking if the relative amount of irradiation is considered. The percentage of patients with irradiation was higher in the group with metastasis in respect to both the carcinomas and the seminomas. Despite this, the survival rates were considerably lower among individuals showing obvious metastasis, demonstrating how serious a prognostic factor is the observation of metastasis.

Survivals according to type and known duration of the lesion before treatment are likewise shown in Table 3. It has long been assumed that relatively early diagnosis is of great importance in prognosis. Table 3 does not very clearly bear out this view. In the group classified as carcinoma, the survival rate over the three-, five- and ten-year periods is somewhat higher for those patients in whom the known duration was less than a year. On the other hand, the difference is small and of doubtful statistical significance.

In regard to the cases of seminoma, the situation is even more confusing. It will be noted that in this group the lesions were divided into those with duration of less than six months, of six months to one year and of one year or more. There is a regularly progressive difference in the survival rates unfavorable to those with lesions of short duration among these three groups. As between the group with lesions of less than six months' duration and that with lesions of six months to a year's duration, the difference is substantial; between the latter and the group with lesions of a year or more the difference is meager. On careful consideration, we think that the apparently less favorable result obtained for the group with lesions of less than six months' duration is probably more apparent than real. One of us (J. B.*) has previously pointed out that in studying the life expectancy of patients with cancer in other regions, the same apparently unfavorable result of early diagnosis appeared. This is perhaps due to the fact that the patients who appear relatively early are likely to have what we are pleased to call very malignant lesions. In this series, for instance, we find some substantiation of this theory in the fact that the groups with lesions of longer duration contain a somewhat smaller percentage of patients showing metastasis. This is of course another way of saying that the relation of the cancer to the host is weighted in favor of the cancer. The patients who do not present themselves for a year or more thus represent a certain survival group who, for some mysterious reason, are better able to resist the disease. Nevertheless,

Table 4. *Twenty-Year Survivals.*

Case No.	Year of Treatment	Age	Pathological Report	Last Report	Duration of Life Following Treatment
		yr.			*yr.*
1	1910	36	Seminoma; no metastasis.	Living	27
2	1910	24	Adenocarcinoma, Grade 3 (not a seminoma and apparently not in a teratoma); no metastasis.	Living	26
3	1911	27	Adenocarcinoma, Grade 2 (not a seminoma); no metastasis.	Living	26
4	1912	46	Seminoma; no metastasis.	Dead, "leukemia"	25
5	1912	38	Seminoma; no metastasis.	Living	25
6	1917	52	Seminoma; no metastasis.	Living	20

*Unpublished data.

so far as the figures go they suggest that we must consider the possibility that very early diagnosis is not of the overwhelming importance which has been suggested.

Twenty-Year Survivals

Finally, Table 4 shows a group of 6 cases in which the patients survived more than twenty years. Of the lesions, 4 were classified as seminomas and 2 as adenocarcinomas. None of the patients with seminoma had known metastasis. The adenocarcinomas were classified respectively as Grade 3 and Grade 2 lesions; these patients also had no known metastases. These cases are presented only as evidence that, in the absence of metastasis, a small group of patients will survive even without irradiation.

SUMMARY

This study is based on a follow-up of 363 patients with tumors of the testis seen at the Mayo Clinic between 1910 and 1937. Of this number, 215 were seen only after the diagnosis had been made elsewhere, and in some cases after part of the treatment had been carried out. In order to deal only with patients whose condition was completely observed and treated at the clinic, cases of this type were selected for careful study.

Of these 142 patients, in 59.2 per cent the tumors were classified as seminomas; in 34.5 per cent as adenocarcinomas of various forms; in 6.3 per cent as miscellaneous types of cancer.

The ten-year survival rate of patients having seminoma was found to be relatively high as compared with what is, we think, the commonly held opinion. Thus, 47.4 per cent were alive and apparently well ten years or more after treatment. This should be compared with the survival rate of the patients classified as having carcinoma, which was 26.4 per cent.

The survival rate of seminoma is much higher than that of carcinoma at five years, being 67.7 per cent as compared with 29.3 per cent.

Irradiation seems to materially improve the three- and five-year survival rates for seminoma. Thus, of the patients treated by orchidectomy followed by irradiation, the survival rate at three years was 80.0 per cent, as compared with 68.4 per cent of those not treated by irradiation. At five years the survival rate was 71.1 per cent of the irradiated cases, as compared with 58.8 per cent of those not so treated. Irradiation does not appear to have any important effect on the survival rate at ten years or over. Of the patients treated by irradiation, 47.9 per cent lived more than ten years, as compared with 46.7 per cent of those not so treated.

Of these 142 patients, 6 lived twenty years or more; 2 had carcinoma and 4 had seminoma, and none were treated by irradiation.

SURVEY OF ALCOHOLIC PATIENTS ADMITTED TO THE BOSTON PSYCHOPATHIC HOSPITAL IN 1937*

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BOSTON

THE alcoholic patients admitted to the Boston Psychopathic Hospital during 1937 comprised almost one fifth of the total admissions. This is a marked increase over 1927 (during the Prohibition Era), when such patients numbered approximately one tenth of admissions. In 1937, patients having serologic syphilis totaled only 8.4 per cent of admissions, while disorders diagnosed as dementia praecox and manic-depressive psychosis numbered approximately 15 and 16 per cent, respectively. Alcoholic patients present points of interest other than their gross number, and it is primarily with these in mind that this survey was undertaken.

In 1937, 382 alcoholic patients were admitted to the hospital; their cases were diagnosed as shown in Table 1.

Table 1. *Diagnoses.*

Diagnosis	No. of Cases		
	Men	Women	Total
Alcoholism without psychosis	123	27	150
Alcoholic psychosis:			
Delirium tremens	103	10	113
Acute hallucinosis	16	3	19
Korsakow's psychosis	3	2	5
Other types	64	17	81
Miscellaneous*	12	2	14
Totals	321	61	382

*Cases diagnosed as psychopathic personality with alcoholism, psychosis with drug addiction and alcoholism, and so forth.

The monthly admission rate of alcoholic patients (Table 2) shows slight peaks in September, June and December, without any obvious explanation.

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As would be expected from the large proportion of Irish in Boston, the Irish alcoholic patients far outnumber all other nationalities. In 1937 there were 190 alcoholic patients of Irish extraction, or approximately half the total alcoholic admissions. The English numbered 58 (15 per cent). Thirty-eight (10 per cent) were of mixed race, while the remainder of the admissions were made up of widely scattered racial groups.

Most of the patients were between thirty and fifty years of age. Three were twenty or younger,

Table 2. *Admissions by Months.*

January	29	July	34
February	24	August	33
March	29	September	40
April	29	October	33
May	32	November	23
June	39	December	36

56 were between twenty-one and thirty, 116 between thirty-one and forty, 148 between forty-one and fifty, 52 between fifty-one and sixty, and 7 were sixty-one or older. The youngest was sixteen and the oldest seventy-one.

As to schooling, 197 patients had not gone beyond the eighth grade; 156 had completed high school and 29 college.

Of the 382 patients, 83 (21.7 per cent) were sent to the hospital on a court order under a specific charge. Only 44 patients (14.0 per cent) were committed to other state hospitals, indicating that the majority of alcoholic psychoses cleared within the prescribed ten-day observation period.

Interesting information is to be obtained from a study of the physical and mental status of the various patients. There were 5 deaths (1.3 per cent), 2 in the delirium tremens group and 3 in the group designated as "alcoholic psychoses, other types." Two deaths were attributed to pneumonia, 1 to poisoning by bichloride of mercury, 1 to cardiac decompensation accompanied by uremia and peripheral neuritis and 1 to circulatory collapse with delirium and exhaustion. Table 3 indicates the number of alcoholic patients with evidence of physical disorder of a specific type. It is evident that neuritis, hepatic disorder (including cirrhosis) and bronchitis far outnumbered other complicating diseases. We ordinarily associate neuritis and hepatic disorder with excess intake of alcohol, and although these disorders were present in 14.0 and 13.0 per cent of all alcoholic admissions, respectively, it is surprising that some clinical evidence of these disturbances was not found in even more cases. Bronchitis was relatively frequent, while pneumonia was an uncommon complication. Only 2 patients died of pneumonia, while 3 recovered. This is to be considered fortunate, since, as is well known, alcoholic patients succumb to pneumonia much more readily than do non-alcoholic ones. Serological tests for syphilis were positive in 14 cases (3.4 per cent). The total admissions of patients with syphilis made up 8.4 per cent of the total hospital admissions for 1937, or more than double the proportion in the alcoholic group.

Table 3. *Varieties of Physical Disorder.*

TYPE OF DISORDER	NO. OF CASES
Peripheral neuritis	55
Hepatic disorder (including cirrhosis)	51
Bronchitis	45
Serologic syphilis	14
Lesions of midbrain and medulla	11
Convulsions (related to alcoholism)	10
Optic atrophy	6
Pneumonia	5
Pellagra	4
Testicular atrophy	4
Ulcer of the stomach	1

Eleven patients showed evidence of lesions in the midbrain or medulla, with cranial-nerve palsies, which in some cases remained only for a brief period, while in others the neurologic findings persisted. Alcoholic patients having cranial-nerve palsies usually showed a mental syndrome consistent with the diagnosis of Korsakow's psychosis, or chronic deteriorative changes, with varying degrees of loss of memory and of behavior disorders. No pathologic material was available for study in this group, as there were no deaths. It seems reasonable to conclude, however, that in an alcoholic psychosis accompanied by cranial-nerve palsies we were dealing with a pathologic process known as the superior polioencephalitis of Wernicke.

It is of interest that 10 patients had convulsive seizures, or what the alcoholic patient commonly refers to as "rum fits." These seemed to be definitely associated with excessive alcoholism, since they occurred only after heavy bouts of drinking. Although convulsions are a relatively uncommon complication of alcoholism, it is well to bear in mind that seizures do occur in this group without any demonstrable evidence of pathologic lesions that would explain the convulsion on some other basis.

Optic atrophy occurred in only 6 cases. It is difficult to say whether there was a direct causal relation between the alcohol and the atrophy. It is well known that methyl alcohol will produce such a change, and that it is seldom found in patients who drink ethyl alcohol. There was no way of ascertaining whether alcohol was primarily responsible for the optic atrophy or whether it was an incidental finding. The same thing was true of testicular atrophy, of which there were 4 cases. There were also 4 cases of alcoholic pel-

lagra, or only 1.0 per cent of the total alcoholic admissions. With neuritis we assume that there has been vitamin deficiency resulting finally in the clinical syndrome of the disease. This is true also of pellagra. It seems strange that more patients did not develop clinical manifestations of both these disturbances, as the dietary history was definitely at fault in many more cases than developed these diseases. It is of interest that only 1 patient in the series had a gastric ulcer — a low incidence which may have no significance for our study.

The urine examinations showed evidence of some form of abnormality (albumin, sugar, white cells, red cells or casts) in 250 cases (68 per cent). In many cases the abnormal findings cleared before the patient had left the hospital.

Eighty-five patients (22.0 per cent) had been in the hospital on previous occasions. Eighty-four had a history of previous psychotic disorder due to alcohol, with no hospital admission. All the patients gave a history of drunkenness on previous occasions. In 5 cases no information as to previous alcoholic disorder was available.

The mental status of the patients in this series shows certain factors of interest. The classic description of a patient with delirium tremens is that of an individual who is fearful and tremulous, and has periods of delirium and confusion associated with visual hallucinations of animals or insects, usually dogs, snakes, rodents or elephants. In this series only 57 patients exhibited any evidence of fear. Visual hallucinations of dogs and insects were the most frequent, occurring in 15 patients. Visual hallucinations of snakes occurred in 14, and those of rodents in only 1, in contrast to the assumed frequency of the latter. Horses appeared in 10 cases, while other animals not specified were seen in 9. Faces were seen by 10 patients, and flashes of light by 10. Birds, cats or dead bodies were noted in 5 cases. Elephants were seen by 4 patients; only 1 patient saw a pink elephant, and in this case the hallucination occurred as a retrospective falsification. Lions and tigers were seen by only 2 patients; whales were seen by 1 and a hippopotamus by 1. There was no correlation between the size of the animal and the duration of the delirium. Hallucinations of smell were present in only 3 cases. Lilliputian hallucinations were experienced by 3 patients. In only 1 case was there an occupational delirium. Forty-eight patients believed that hostile gangs or police were chasing them, the sensation being usually accompanied by visual hallucinations.

Accurate information concerning the duration of the psychosis prior to entry was unavailable, but the duration of mental symptoms after reaching the hospital is shown by our own records. In 198 cases the symptoms had disappeared before entering the hospital. In 72 they were considered chronic; that is, they persisted after a ten-day observation period. In 63 cases they lasted one day; in 25 two days, in 11 three days, in 2 four days, in 1 five days, in 3 six days, and in 1 seven days. The longest episode of delirium tremens in the hospital was seven days. In the great majority of cases the symptoms had either cleared before entry or lasted only one or two days after it. The type of treatment seemed to have little influence on the duration of the psychosis. Some patients who received no drugs or other form of medication cleared as soon as those receiving sedative drugs. Paraldehyde in doses of 3 to 20 cc. was used most frequently, and was of considerable value in the management of acutely excited and delirious patients.

Depression was a frequent symptom, occurring in 89 patients (23.0 per cent). Forty-six of these had attempted suicide while under the influence of alcohol, and 17 others made suicidal threats. Twenty-six patients were depressed without previous suicidal attempts or threats of suicide. The most frequent precipitating factor was domestic difficulty. This may be an important disturbing element, but in many cases it is impossible to untangle cause from effect. In some cases it seems highly probable that domestic friction was the result rather than the cause of the alcoholic episodes. It is of interest that 122 patients (32.0 per cent) were unemployed. This was undoubtedly a contributing or precipitating factor in many cases.

Repressed homosexuality is considered by many to be the principal underlying cause of alcoholism. In this series 17 patients (4.4 per cent) admitted overt homosexuality, but this group included only 1 woman out of a total of 61. In 18 patients (4.7 per cent) there were hallucinations of homosexual abuse. In 48 patients (12.8 per cent), as stated above, there were delusions and hallucinations of being chased by gangs or police. It may be argued that the character of these delusions and hallucinations points, to latent homosexuality, but this seems to place an interpretation on the clinical material which is not warranted under the circumstances. There are undoubtedly many factors which either contribute to or are directly responsible for alcoholic excess.

SUMMARY

The number of alcoholic patients admitted to the Boston Psychopathic Hospital in 1937 almost doubled as compared with those admitted in 1927. This increase was not present among the groups with syphilis, manic-depressive psychoses and dementia praecox. It is not evident why the proportion of

patients having syphilis among the alcoholic group was notably less than that among admissions in general.

The most frequent complications were neuritis, hepatic disorders and bronchitis; pneumonia rarely occurred. There were only 5 deaths (1.3 per cent). It is not readily explainable why more patients did not have neuritis or pellagra, as the diet was deficient in more cases than showed these disorders, and this fact seems to point to a marked individual variation of reaction to similar precipitating factors. Patients showing cranial nerve palsies invariably showed gross intellectual impairment, indicating extensive involvement of the higher brain centers.

Twenty-two per cent of the patients had been admitted on previous occasions. Approximately the same number of patients in this series had had previous alcoholic psychoses without hospital admission. There was no correlation between the type of hallucination and the duration of the psychosis. The most frequently occurring visual hallucinations were those of dogs and insects. Lilliputian hallucinations and occupational delirium were unusually rare. The number of depressed and suicidal patients in this series is noteworthy and deserves a more thorough investigation. Homosexuality, either overt or latent, was discovered in surprisingly few patients.

The etiologic and precipitating factors of alcoholic excess are most complex, and it seems that no single explanation will fit all cases.

REPORT ON MEDICAL PROGRESS

MEDICAL ASPECTS OF OBSTETRICS

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THIS article presents a sabbatical survey (since 1932) of progress in those aspects of practical obstetrics which may fairly be denominated medical rather than surgical, and leaves for a complementary review those aspects of the specialty which are of importance from the surgical standpoint. Since editorial policy calls for information of the broader aspects of progress, tempered with critical comment, rather than for a meticulous review of current literature, the writer has avoided, so far as possible, quotations of chapter and verse in favor of a concentrated summary of various important subjects.

PHYSIOLOGY

From a practical aspect, rhythm as a means of promoting or inhibiting pregnancy can undoubtedly be used successfully by many couples for long periods. Several authors both in Europe and in America have published clinical tabulations of many thousands of copulations during the "safe" period with complete avoidance of undesired pregnancies. These figures, however, convincing so far as they go, do not answer the logical objections that the human race is not yet sufficiently disciplined to regulate its emotional urges by the calendar; that variations in the time of ovulation in the cycle may occur, as evidenced by unpredictable prolongations of the estrin or corpus-luteum phases; and that the possibility of induced coital ovulation as an unorthodox occurrence in human biology cannot be entirely disregarded.[1]

Sex regulation of human offspring seems, by analogy with animal genetics, to be linked with the sperm cell which fertilizes the ovum. A theory that relative alkalinity of the vagina at the time of intercourse results in a preponderance of male children has been advanced, suggesting the use of sodium bicarbonate by douching or instillation before coitus if the birth of a boy is desired. This theory, advanced in the German literature before the rise to power of the present chancellor, has subsequently, and possibly to the disappointment of *Der Führer,* remained unsupported by other investigators.

Prediction of sex in the unborn child has been attempted by various biological methods. Most attention has been paid to acceleration of spermatogenesis in the testicles of three-month-old rabbits following the injection into the test animal of urine from women in the second half of pregnancy.[2] Though the original investigators of the test reported successful prediction of sex of the child in 80 of 85 cases, later investigators were unable to obtain confirming results.

The two preceding paragraphs indicate that no reliable method has yet been devised either to regulate or predict the sex of the human infant.

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DIAGNOSTIC TESTS

Diagnostic tests for early pregnancy have been sifted down to a clear acceptance of the Aschheim–Zondek (mouse) and Friedman (rabbit) tests as the most reliable. Either test, when done by reliable technicians, will give a positive reaction in 98 per cent of normal pregnancies,[3] and will give an equal ratio of negative reactions in patients who are not pregnant. No other test yet described, chemical or biological, approaches these two in accuracy. When, however, evidence is required in pathologic pregnancies as to the status of the fetus in utero, for example in estimating the prognosis for the child in threatened abortion, or in cases where intrauterine death of the fetus is suspected, these tests must be looked on with caution. For example, in a patient known to be pregnant who has shown some vaginal bleeding, a repeatedly negative test would indicate death of the entire ovum, both fetus and appendages; if, however, the test is positive it is so because of endocrine activity of the still functioning trophoblast or placenta, and this cannot be adduced as an indication that pregnancy will continue successfully. In hydatidiform mole, moreover, the test is characteristically strongly positive, and becomes so again even after clinically complete evacuation of the mole if chorion epithelioma ensues. Finally, in the case of suspected ectopic pregnancy, the test, though valuable as confirmatory evidence if positive, does not in any way rule out the diagnosis if negative, as early death and degeneration of the ovum is the rule in this condition.

In summary it may be said that while in normal pregnancies the Aschheim–Zondek and Friedman tests are of great diagnostic aid, especially before the clinical signs are unmistakable, in pathologic pregnancy the wise clinician will evaluate his test findings on the assumption that they indicate the presence or absence of functioning trophoblastic tissue, either in the uterus or elsewhere.

METABOLISM AND NUTRITION DURING PREGNANCY

Much attention has been paid in the literature to the metabolic and nutritional aspects of pregnancy. The routine weight chart of the patient is quite as important a part of prenatal care as are the blood pressure and urinalyses. Evidence has been accumulated in increasing volume that attempts to control the weight of the fetus at birth by regulating the weight of the mother are only partially successful. On the other hand, excessive increase in maternal weight, especially during the last three months of gestation, often due to mild or even subclinical edema, is a valuable sign of the insidious onset of hypertension or albuminuria or both.[4]

Metabolism of minerals and vitamins has been the subject of numerous papers. The addition of iodine to the diet in the form of syrup of hydriodic acid, five drops every other day, is believed by some to be of value to the pregnant woman in the goiter areas of the country, by lessening the incidence of congenital goiter and cretinism in infants. Lugol's solution, given by rectum and subcutaneously, has been advocated in the treatment of certain cases of vomiting of early pregnancy in which an underlying hyperthyroidism may exist.

An adequate intake of calcium and phosphorus in the form of one quart of milk, a liberal helping of green, leafy vegetables and a serving of meat at one meal, with the addition to the diet of an egg per day, is ordinarily amply protective so far as the maternal supply of these elements essential to the fetus is concerned. During the early phases of pregnancy, when "physiologic" nausea is common, it may be impossible to induce the prospective mother to take a properly adequate diet: fortunately, however, the fetal demands reach a peak during the last months of gestation, when dietary whims are much better controlled by advice and suggestion.

It is important at this point to consider vitamin D as the catalyzer of calcium and phosphorus metabolism. Since it is of scanty occurrence in most "natural" foods, many clinicians prescribe it in the form of cod-liver oil or viosterol in the routine diet of pregnant patients, in order to ensure an adequate supply of calcium and phosphorus both to the maternal teeth and to the fetal skeleton. It is claimed by some that the muscular cramps which are so common in pregnancy are relieved by viosterol or inorganic calcium or both. Since, however, no convincing evidence has yet been adduced either that the maternal dental structure requires these supplements, or that the infant will fail to receive its normal skeletal requirements if these additions to the mother's diet are not made, and since premature ossification has been reported in fetus and placenta following large doses of vitamin D in pregnancy, the situation as summarized by Stander[6] is worthy of repetition: "Should it be necessary, because of dietary deficiencies, inability to drink milk, or lack of sunshine, to supply compounds of calcium and phosphorus, and vitamin D, these must be administered with care, certainly in respect to vitamin D, as overtreatment may be as injurious as the deficiency itself."

There is very little belief at present that even in toxemic pregnancy the diet should be low in protein; in fact, a small group of toxemic patients with the nephrotic syndrome should have a liberal protein intake. To place a pregnant patient

on a meat-free diet is to invite the development of hypochromic anemia, and in certain cases to reduce the plasma proteins to an edema level. The ingestion of table salt, however, is a different matter, since an oversupply of the sodium ion, whether in the form of sodium chloride or of sodium bicarbonate, as taken immoderately by many women to combat flatulence and heartburn, tends to bind fluids in the tissues, thereby producing edema in the last trimester of pregnancy, when the ability of the kidney to excrete a highly concentrated urine is distinctly below normal.

The problem of vitamin adequacy in the diet of the pregnant woman has been widely discussed, and is still a somewhat controversial subject. For practical purposes a diet which contains milk, fruits and green and yellow vegetables each day and liver once or twice a week should be adequate for vitamin A; whole-wheat bread and whole-grain cereals will supply vitamin B_1; liver, buttermilk and lean meat are good sources of vitamin B_2; adequacy in vitamin C is assured by the daily ingestion of 6 to 8 ounces of orange juice, grapefruit juice or tomato juice. Vitamin D has been discussed above. Vitamin E is supplied by lettuce and wheat germ. Inadequacy of this substance has been claimed to result in abortion in the early months of pregnancy[7] and ablatio placentae in the last trimester,[8] and its routine administration in the form of wheat-germ oil has been advocated as a prophylactic against these conditions. The routine use of the substance, however, must be accepted with reservations, as the dosage is still empirical and the effects of overdosage are little if at all understood.

The hemoglobin content of the blood in pregnancy, especially in its latter half, is usually below normal. While this is undoubtedly due in part to the demonstrated increase in plasma volume which takes place at this time, it is nevertheless a fact that an actual anemia often occurs. This anemia has been postulated as due either to a direct dietary deficiency or to one conditioned by gastric anacidity, hypoacidity or associated defects, in the presence of fetal demand for blood-building material.[9] Microcytic (hypochromic) and macrocytic (hyperchromic) types have been described, the former occurring much more frequently than the latter. Ferrous sulfate, 9 to 12 gr. daily, added to the diet is sufficient to combat hypochromic anemia, while liver or liver extract, with or without the addition of iron, controls the macrocytic or Addisonian-like type.

HYPEREMESIS GRAVIDARUM

While the etiology of hyperemesis gravidarum remains obscure, several points in the diagnosis and treatment deserve comment. Toxic neuritis or neuronitis as a concomitant of prolonged or severe cases has been described, with a mortality of about 25 per cent in this group. Attention has been directed to the administration of vitamin B_1[10] by duodenal tube or parenterally, both prophylactically and therapeutically, in severe cases. Suprarenal cortex has also been advocated, but the original results on which this recommendation was based have not been repeated uniformly elsewhere. The administration of Lugol's solution by rectum or by the hypodermic route has been mentioned above. The procedure, however, of feeding fluids, calories and accessory vitamin factors B_1, B_2 and C by duodenal tube has proved to have great value in severe cases, provided always that strict isolation of the patient from relatives and friends, preferably in a hospital, is observed.[11]

PREGNANCY ASSOCIATED WITH PULMONARY TUBERCULOSIS

Opinions still differ, as always, regarding the relative advisability of interrupting pregnancy in the tuberculous woman and of allowing the gestation to proceed to term. The general trend of thought is toward allowing the tuberculous gravida to continue in pregnancy, provided she has sanitarium observation and care or its equivalent; this is tantamount to ruling that the case be studied and cared for by the expert in tuberculosis, working in co-operation with the obstetrician. Pneumothorax in pregnant women is quite as feasible, if properly done, as in non-pregnant women, and recourse to this measure may enable many patients to go safely through pregnancy who could not otherwise do so. Floyd[12] seems to strike a sane middle ground in the management of the associated conditions when he advises the following measures:

For the case with healed or obsolete lesions, continuance in pregnancy under sanitarium precautions in the home.

For the case with early active lesions, the same with pneumothorax.

For the case with well-established tuberculosis, pneumothorax at once, otherwise therapeutic abortion.

For the advanced case with a poor prognosis from tuberculous standpoint, continuance in pregnancy for the benefit of the infant.

For the case with miliary infection, neither pneumothorax nor abortion, as neither procedure improves the prognosis.

PREGNANCY ASSOCIATED WITH DIABETES MELLITUS

Because of the control of diabetes by insulin, more diabetic women are able to conceive and bear children than was ever possible in the pre-insulin era. The essential factors in the successful management of such cases are close control of the diabetes by means of diet and insulin, the skillful

treatment of intercurrent infections and a close watch for the development of toxemic conditions. If this ideal is to be attained, each case should be followed by the internist and obstetrician, working in conjunction. Contrary to the theory that the pancreas of the fetus helps the maternal metabolism, experience seems to indicate that, in many cases at least, the diabetes becomes more severe during pregnancy, and requires a higher dosage of insulin for its control as pregnancy advances. The occurrence of hyperemesis in the first trimester may make control of the disease impossible, while during the last trimester, toxemia and eclampsia seem to be more frequent than in nondiabetic pregnancies. Despite improvement in the maternal risk, the fetal wastage is still higher than one would like to see it. Whether or not in the long run better fetal results will be obtained by routine abdominal section as soon as the infant is deemed viable,[13, 14] or by reserving section only for over-large babies and ordinary obstetrical indications,[15] is still a controversial question.

PREGNANCY ASSOCIATED WITH CARDIAC DISEASE

It has been taught for many years on clinical grounds that the gravid state throws an extra burden on the circulatory system. Quantitative evidence obtained in the laboratory which has tended to rationalize this view is gradually being confirmed by observations made on living pregnant and parturient women. Thus, considering the finding that cardiac output rises to 50 per cent above the normal volume with advancing pregnancy, the finding that total blood and plasma volumes in the circulatory system also increase, and the frequency of rises in the systemic blood-pressure and pulse rate as gestation advances, no matter to what extent these processes are mutually causative, the increased burden on the circulation is evident.

That normal hearts and blood vessels adapt themselves to this strain is remarkable. That the damaged heart of the cardiac patient can bear this burden is often in doubt. The mere diagnosis of valvular heart disease does not give definite evidence of the organ's incapacity to withstand pregnancy, as many women with mitral stenosis or aortic regurgitation or a combination of the two may go through pregnancy and labor without any untoward event; some, on the other hand, have cardiac failure. Functional tests such as dumbbell-swinging, stair-climbing, and so forth, may reveal imminence of cardiac decompensation, but may give false assurance that the Class 1* patient can reasonably be expected to stand the burden of advancing pregnancy. It seems much more logical to believe with Hamilton[16] that the patient with a diastolic murmur, an unmistakable enlargement of the heart or both should be classed as an unqualifiedly bad risk for pregnancy if she has signs or history of decompensation, or if she has in addition auricular fibrillation; and to look upon her as a *relatively* favorable risk if fibrillation or signs or history of decompensation are absent; not, however, losing sight of the possibility that either of these conditions may arise despite strict medical supervision. A favorable cardiac case, classified on this basis, should have a 2 per cent mortality risk; an unfavorable case has been shown to have a 16 per cent risk, whereas one with auricular fibrillation courts a 33 per cent mortality.

Clinical evidence has accumulated that the peak load for the cardiac patient occurs toward the end of the sixth, during the seventh and at the beginning of the eighth month of pregnancy. Should the eighth month be passed without failure, the chances of decompensation during the ninth month or during delivery appear to be relatively small. Evidence has been adduced that the cardiac patient has neither a shorter and easier nor a longer and harder labor than the woman with a normal heart. The present trend is distinctly in preference of delivering favorable cardiacs through the pelvis at term, and of reserving abdominal section for those cases in which a purely obstetric indication exists.

The unfavorable cardiac, on the other hand, requires a different approach. She should, if contemplating pregnancy, be warned of the risk involved. If in early pregnancy, she should be allowed the option of abdominal abortion and sterilization. If, as often happens, she has started pregnancy as a favorable risk but later, because of decompensation, becomes unfavorable, the immediate treatment should be hospitalization, complete bed rest and intensive efforts to restore compensation. This regime, sometimes unavailing, is at best time-consuming, but often tides women over the seventh and eighth months, following which, with the peak load diminishing, the restored compensation allows a surprising proportion of these cases to be delivered safely through the pelvis.

In summary, it seems that the chief advances in the management of pregnancy complicating heart disease during the past seven years are largely the results of accurate classification of patients with seriously damaged hearts; the prognosis, according to classification, of the risks inherent in pregnancy and labor; and the relegation of abdominal section to a minor role in the obstetrical management of the favorable cardiac.

*New York Heart Association and American Heart Association classifications.

HYPERTENSION AND ALBUMINURIA, EXCLUSIVE OF ECLAMPSIA

A survey of seven years reveals little if any progress in the discovery of a single background which suffices to explain the occurrence of these toxemic conditions. Claims have been made that a vicious cycle may be started in the second half of pregnancy by an oversupply of fluids to an individual whose renal capacity for water excretion is physiologically depressed, and that this cycle may proceed to a generalized edema which, acting on the central nervous system, may result in eclamptic convulsions and coma. The work of certain investigators pointing toward an etiology based upon increased activity of the posterior pituitary, through which they explain edema and oliguria by antidiuretic action of the hormone, and hypertension as the result of the pressor action of the same incretion, has not been confirmed by others. Retention of sodium ion resulting from an oversupply of sodium salts or from the inability of the kidney to excrete a concentrated urine has had its advocates as an important etiologic factor. Another endocrine background has been noted by investigators who find excessive amounts of prolan in the blood, urine and placenta of toxemic patients, with a tendency toward a depression of the estrin level from the same sources. A recognized or unrecognized pre-existing pyelitis or pyelonephritis, it has been claimed, sets the stage for the subsequent development of toxemia during pregnancy. Finally, changes in the placenta, with infarction of this organ resulting in the elaboration of protein split products, such as guanidine, are looked upon by some as the causative factor. Strangely enough, very little is said concerning the ancient bugbear of nitrogen retention resulting from a diet supposedly too rich in protein.

From the standpoint of classification some progress has been made. Certain patients showing evidence of disease independent of pregnancy may be identified as having vascular hypertension, nephrosis or nephritis. Most cases, however, as first seen during pregnancy, give no history and yield no evidence of disease, so far as the physician can learn at first glance, independent of the pregnant state. These are divided into two categories: low-reserve kidney, according to the classification[17] of the Johns Hopkins Hospital, or pre-eclampsia, Grade 1, by the standards of the Boston Lying-in Hospital;[18] and pre-eclampsia (Johns Hopkins Hospital) or pre-eclampsia, Grade 2 (Boston Lying-in Hospital). The dividing line between the two is more or less arbitrary, and consists in the degree of hypertension or albuminuria or both; prodromal symptoms and signs suggesting impending eclampsia are limited to the second group.

Despite the admitted uncertainty of the etiology of the toxemias of late pregnancy, and the numerous recently published studies of blood chemistry and renal function, certain basically important measures in the treatment of these conditions may be stated as within the scope of any physician who practices obstetrics:

Constant control of the pregnant patient by watchful interpretation of her symptoms and changes in her blood pressure, urine and weight.

Increased surveillance, even to hospitalization, should hypertension, albuminuria or both appear.

Salt-poor or salt-free diet, restriction of fluids by mouth, bed rest, moderate saline catharsis and strict watch for rising blood pressure or increasing albuminuria after the above signs appear.

Interruption of pregnancy should hypertension be unchecked, albuminuria increase or nervous symptoms suggesting impending convulsions appear after the above regime is instituted.

ECLAMPSIA

This condition remains a "disease of theories." Both in its temporal relation to pre-eclampsia (Grade 2) and in its blood picture it is undoubtedly more closely allied to the latter condition than to nephritis, even though it often leaves impaired kidney function as a sequela after pregnancy has terminated. Closely allied though pre-eclampsia and eclampsia may be, it is important to recognize that the pre-eclamptic patient who becomes eclamptic exchanges a 2.5 per cent risk of death for one of 25 per cent;[18] hence the dictum that eclampsia is better prevented than cured.

Recent experience convinces us of several points in the treatment of this condition:[19]

Broadly speaking, the essence of a successful result lies in conservative treatment aimed at controlling the convulsions.

Conversely, immediate delivery by any means, above all by abdominal section (save in the rarest individual case), should be strongly deprecated.

Hospitalization and special nursing, if available, provide an environment more favorable than the home.

Morphine as a medication for control of convulsions *may* be better replaced by barbiturates administered by mouth or, in comatose patients, by rectum or intravenously, as an immediate or emergency measure.

Magnesium sulfate given intravenously, 20 cc. of a 10 per cent solution, will control the convulsion, and repetition of this dose to the extent of 60 to 80 cc. in twenty-four hours may be safely carried out if repeated convulsions occur or impend.

Frequent examinations or colonic lavage may excite further convulsions.

Hypertonic glucose solution given intravenously is advantageous in combating oliguria and anuria.

If labor ensues following convulsions, Nature has been kind. If the convulsions have been well controlled, induction of labor by rupture of the membranes is advisable.

PUERPERAL INFECTION

Certain important elements in the prophylaxis and treatment of puerperal septic infections deserve consideration.

There has in the past few years been a marked stimulus to the obstetric conscience in the realization that the original focus of many cases of intrapartum as well as postpartum infection lies in the nasopharynx of an attendant. The idea is not new, and it has been frequently stressed since it was called to the attention of the profession in a clearly written article by Watson and his associates[20] in 1928. The presence of infectious organisms in the noses and throats of physicians, nurses and other hospital attendants is quite as common as in the population at large, and their insidiousness lies in the fact that no clinical symptoms may be present in the host: in other words, *everyone is a potential carrier.* As an obvious corollary, every person in attendance on a woman at delivery, and every nurse performing the perineal toilet of a postpartum patient, should, in addition to scrupulous care in digital asepsis, be effectively masked as to nose and mouth. In addition, every person known to be a carrier of the hemolytic streptococcus should be rigidly excluded from delivery or nursing care of the obstetric patient until such time as absence of the organisms is assured.[21]

The therapy of puerperal infection has been greatly advanced by the work of Colebrook and his associates in England, and by Long, Keefer and others in this country. The first-named group,[22] using Prontosil by oral, intramuscular and intravenous routes in 64 puerperal cases of infection with beta hemolytic streptococci, and later administering the allied substance sulfanilamide, usually by the oral route alone, to 100 other cases, were able to report a reduction in mortality in streptococcal infection from 23 per cent in the preceding five years to 5 per cent since early 1936. Keefer[23] reports that sulfanilamide used in treatment of puerperal sepsis due to streptococci prevents the local process from spreading, and inhibits invasion of the blood stream. In his experience in cases with bacteremia, with or without peritonitis or extensive thrombophlebitis, mortality has been reduced from 70 to 40 per cent.

A formidable amount of literature dealing with the effect of sulfanilamide on all types of streptococcal infections has appeared. Evidence indicates that the drug is bacteriostatic rather than bacteriocidal or antitoxic, and that its best effects are obtained in those cases which have some power of mobilizing an immune reaction against the invading organism.

Despite the fact that sulfanilamide provides us with a potent therapeutic measure against the most dreaded agent of puerperal infection, a word or two of caution should be mentioned. Not all forms of sepsis are benefited: the drug is most active against the beta hemolytic streptococcus, but certain strains of this organism are resistant to its action; against the staphylococcus it has relatively little effect. Sulfanilamide therapy, to be effective, requires heavy dosage of the drug, with control determinations of the percentage level of the substance in the blood stream. Malaise and cyanosis are almost universal. The hemoglobin and red- and white-blood-cell counts should be determined at least every two days or better every day, because mild hemolytic anemia is common, and acute hemolytic anemia and agranulocytosis occur occasionally, as toxic manifestations. A fever due to the drug itself occurs in 9 per cent of the cases, according to Long,[24] and is an urgent indication for omission of the therapy.

It seems fair to conclude that the use of sulfanilamide in puerperal infection is an effective, though somewhat two-edged, measure. The physician prescribing it will be well advised to draw no conclusions concerning his results unless they are bacteriologically controlled, and unless they are obtained under the most scrupulous clinical observation, aided by adequate laboratory investigation.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 25051

PRESENTATION OF CASE

A fifty-four-year-old married insurance agent entered complaining of abdominal swelling of two weeks' duration.

He was perfectly well until six or eight months before entry when he first noted weakness and lack of force in his urinary stream. There had been no dribbling or difficulty in starting or stopping the flow. Since then he had nocturia once each night. One month before entry he noticed swelling of his left leg which came on during the day and subsided at night. During the following week the edema gradually became generalized, involving the face and hands. Enlargement of the abdomen developed two weeks before entry. This gradually increased, causing respiratory embarrassment and a sensation of fullness in the chest. He had had chest pain, alternating from side to side on inspiration, without other symptoms during the previous winter, but had had no dyspnea or edema at any time before the onset of the present illness. No cough, sputum, anginal pains or palpitation had been noted. His urine had become somewhat hazy but there was no change in color. During the past two weeks he had been confined to bed and fed only liquid food. His appetite was good, and he had had no previous nausea, vomiting, malaise, chills or fever. His bowel movements had been regular and of normal color. After being confined to bed, however, he had had nausea and vomiting on two consecutive nights. The vomitus contained no trace of blood or bile. He had gained 10 pounds in weight. His past and family histories were noncontributory. He had had his gall bladder removed twenty-three years previously.

Physical examination showed a well-developed and nourished man having some difficulty in breathing. Pitting edema was present over the entire body. The tongue was coated. The diaphragms were high on both sides, but examination of the lungs was negative. The heart was not remarkable. The blood pressure was 130 systolic, 84 diastolic. There was marked abdominal distention, and tympanites with shifting dullness in the flanks. No tenderness was present, and no masses could be palpated. There was an old cholecystectomy scar in the right upper quadrant.

The temperature was 97.8°F., the pulse 90, the respirations 20.

The urine was amber colored and acid in reaction, with a specific gravity of 1.034, a large trace of albumin, many hyaline casts and an occasional red cell and 3 to 5 white cells per high-power field. The blood showed a red-cell count of 4,970,000, 90 per cent hemoglobin, and a white-cell count of 15,500 with 90 per cent polymorphonuclears. The serum nonprotein nitrogen was 40 mg. per cent, the protein 4.5 gm. The chlorides were equivalent to 85 cc. N/10 sodium chloride. A blood Hinton test was negative.

X-ray films showed a large abdomen containing fluid. The right kidney outline was visible and not definitely abnormal; the left was not seen. The gas shadows in the bowel were not abnormal. There was no evidence of abdominal tumor. The diaphragm was high on both sides, particularly on the right. An area of density, apparently fluid, partially obscured the outline of the diaphragm and obliterated the right costophrenic angle. The left lung was clear. The heart and mediastinum were not remarkable.

On the day after admission two midline paracenteses failed to evacuate any fluid except a few blood-tinged drops which might have come from the edematous abdominal wall. That night the right leg and arm suddenly became numb, the fingers of the right hand crossed and could not be moved, and he was unable to move his arm or leg. He had fleeting pains in the left chest. These symptoms passed away within a few minutes, and he was again normal. On the fourth day his edema had increased and involved the right leg more than the left. Erythema appeared on the right leg and lower abdominal wall. The skin of these areas was very sensitive. Salyrgan and ammonium chloride therapy caused no diuresis. On the seventh day digitalization was begun. The urine showed no Bence-Jones protein. The serum nonprotein nitrogen was 40 mg. per cent, and the cholesterol 317 mg. An electrocardiogram the following day showed a P-R interval of 0.2 seconds. There was no evidence of myocardial damage. Urine examinations during the next three days all showed a specific gravity of 1.016, a trace to a large trace of albumin and a rare red blood cell and 2 to 3 white blood cells per high-power field. One specimen showed many finely granular casts. A stool was guaiac negative. The blood white-cell count was 11,100.

On the eleventh day the serum protein was 4.4 gm. per cent. The following day the patient

showed marked weakness, slight cyanosis, nausea and vomiting. The vomitus gave a 3+ guaiac test. His blood pressure was 110 systolic, 90 diastolic. Moist rales were heard at both lung bases. Following a transfusion the patient seemed slightly improved, but the following day was weaker than ever. On the fourteenth hospital day respirations were shallow, the pulse weak and thready, the blood pressure 80 systolic, 50 diastolic, and the temperature 96°F. His condition rapidly became worse, his pulse and blood pressure were unobtainable, the fingertips became cyanotic, and respirations were labored. An oxygen tent, intravenous dextrose and other stimulants had little effect, and the patient died that afternoon.

Differential Diagnosis

Dr. Bernard M. Jacobson: I do not believe that we can consider the generalized edema and ascites as due to heart failure on the basis of arteriosclerotic heart disease with congestive failure. He had no symptoms suggesting such a diagnosis and no physical signs referable to the heart. The question might be raised whether we could consider this nutritional edema either dependent on protein deficiency over a long period of time or due to a beriberi type of heart failure with generalized edema. Against these two rare possibilities is the fact that he is reported to be well nourished. Apparently he ate well during the month before admission, and there was no alcoholic history, polyneuritis or massive amount of protein in the urine. On the other hand, it seems to me that we have most of the evidence needed for a diagnosis of primary renal disease. We have a story of previous nocturia over a period of six to eight months and of generalized edema reinforced by a gain of 10 pounds in weight, in spite of not being up to par before entry. The principal findings consisted of generalized edema, marked ascites and possibly fluid in the pleural cavities. The laboratory findings were also consistent — a high specific gravity and massive amounts of albumin and many casts in the urine. The serum protein was low, and the serum cholesterol high, 317 mg. The rather low value for the serum chlorides, 85 milliequivalents, is not the rule in chronic parenchymatous nephritis with edema, but it does occur. We are not told whether the plasma bicarbonate was determined. We should expect it to be high if the chlorides were really low. Of course the chloride deficit in the blood might well depend on previous vomiting and poor chloride intake. The determination, however, was apparently not repeated.

"On the day after admission two midline paracenteses failed to evacuate any fluid except a few blood-tinged drops which might have come from the edematous abdominal wall." I do not know how to explain that in view of the very definite physical findings of ascites.

"That night the right leg and arm suddenly became numb, the fingers of the right hand crossed and could not be moved, and he was unable to move his arm or leg." A very curious symptom which is not mentioned later in the record, so I assume that it disappeared in the course of a short time. It suggests carpopedal spasm, possibly due to some form of tetany. Was the tetany due to a calcium deficit in the blood? I do not believe so. It is not very usual to see so low an amount of ionized calcium in a person with marked renal disease. Could it have been due to high plasma-bicarbonate accompanying low blood chlorides? It is possible. I doubt whether it was a cerebral vascular accident because it cleared so rapidly.

We get no further information about the progress of the erythematous area on the right lower abdominal wall. One wonders whether it could have been erysipelas or an erysipeloid infection. One speculates as to whether there was a phlebitis. Since it is not mentioned again, I do not believe it warrants further consideration. With all these symptoms and physical signs, I do not see how we can get away from terminal cardiac failure, but I have already mentioned reasons why heart failure cannot be considered as the primary cause. Everything points to chronic renal disease as the background of the entire picture.

Of the types of renal disease this might be, certainly the commonest is chronic glomerulonephritis with edema — the nephrotic stage of chronic glomerulonephritis. It is rare to see such a marked number of casts in urine from a case of amyloid disease of the kidney. We have no history to suggest amyloid disease, and the only cases of idiopathic amyloid disease I have ever seen have had very definite signs of infiltration of the liver and spleen as well.

Is this myeloma involving the kidney, in view of the fact that the urine was examined for Bence-Jones protein? It seems unlikely. Is this acute glomerulonephritis? I doubt it. Against it is the lack of hypertension, the lack of very much sediment in the urine or very many red blood cells and the lack of a marked degree of nitrogenous retention in the blood. My diagnosis is chronic glomerulonephritis, with edema and terminal congestive heart failure.

Dr. Francis T. Hunter: When I saw this man, very little laboratory work had been reported. He had a blood nonprotein nitrogen which was not very high — 40 mg. per cent — and had had three urine examinations. The lowest gravity of the

urine was 1.016, and the highest 1.034. It certainly did look like a nephrotic picture, but as I recall, some years ago we had an individual just like this who was given digitalis because it would not do him harm, and promptly lost all his edema. The question was brought up whether he ought to be transfused, despite a red-cell count of 4,900,000. I think it was right to rule out any possibility of cardiac failure first because, if he had had it, transfusion would have been the worst thing that one could have done for him. Subsequently the electrocardiogram turned out to be negative, and it was rather obvious in a short time that the cardiac situation played no part in his picture.

Dr. Richard Clark: What did his prostate feel like?

Dr. Hunter: I doubt if one could tell on account of the edema. He had the most amazing legs I have ever seen. They were covered with big patches of erythema. It was more like a cellulitis, almost ready to burst. The edema was worse in the dependent part of the body than higher up.

Dr. Robert S. Palmer: If this is a nephrotic phase of a glomerulonephritis, what happened to the red area in the abdomen? Such cases often die of some intercurrent infection.

Dr. Tracy B. Mallory: At the time of autopsy there were none present. Erythemas often disappear post mortem.

Clinical Diagnoses

Chronic nephritis, nephrotic stage.
Congestive heart failure.

Dr. Jacobson's Diagnoses

Chronic glomerulonephritis, nephrotic stage.
Congestive heart failure.

Anatomical Diagnoses

Acute nephrosis, albuminoid type.
Acute pulmonary edema.
Peripheral edema.

Pathological Discussion

Dr. Mallory: The autopsy showed this very generalized edema which had been noted. The principal reason the abdominal taps were negative was that the peritoneum did not contain any ascitic fluid. The abdominal wall was extremely edematous and made the abdomen seem swollen. The pleural cavities were also dry, although the lungs were quite edematous. The heart was normal in size; the coronary arteries and adrenals were negative. The myocardium was normal. The significant positive finding was a pair of very much enlarged kidneys, weighing 500 gm. They were reddish, rather than yellow, but rather pale. When the capsule was incised the parenchyma bulged out over the capsule indicating that the cortex was quite swollen — it measured about 9 to 10 mm. in thickness. On microscopical examination the glomeruli showed surprisingly little. He was, after all, in his fifties, and perfectly normal glomeruli could hardly be expected. There was a trace, perhaps, of thickening of the capillary walls here and there, but I am sure no more than the average man of fifty would be apt to show. In an occasional glomerulus one could find a few more leukocytes than usual but they were not very numerous; I do not believe we found more than 10 in any glomerulus. Although I can imagine a great deal of difference of opinion between histopathologists, I should say the glomeruli were essentially negative. The tubules, in contrast, showed an extreme grade of degeneration. All the cells of the convoluted tubules were greatly swollen and the fuchsinophil granules were frequently swollen to nine or ten times the normal diameter. It is the so-called albuminoid degeneration that is very characteristically seen in nephrosis. To find this type of kidney disease in a five- or ten-year-old child would not surprise me very much, but I have never before seen it in a fifty-four-year-old man. It comes as near to pure nephrosis as I have ever seen. I do not know why he died. He was obviously not uremic. He unquestionably had some degree of infection but did not have a positive blood culture. The head was negative.

Dr. Hunter: Perhaps the transfusion was bad for him.

Dr. Mallory: At any rate it was not a "transfusion" kidney.

Dr. Jacobson: Was there any lipoid?

Dr. Mallory: Practically none whatever. There were very slight deposits in an occasional tubule but not in the tubules that showed the most marked swelling and degeneration.

A Physician: Was the carbon-dioxide combining power of the blood determined?

Dr. Hunter: No.

Dr. Thornton Scott: Was the pulmonary edema sufficient to cause death? He seemed to die a respiratory death.

Dr. Mallory: There was certainly a considerable grade of pulmonary edema. His lungs were heavy, weighing 1600 gm. On the other hand, with fatal pulmonary edema the weight usually goes up to 2000 gm. or more.

Dr. Richard Chute: What do you mean by a "transfusion" kidney? What does it look like?

Dr. Mallory: If a mismatched transfusion is given, hemolysis is produced and the hemoglobin

is excreted through the kidneys. In the course of that process it apparently causes a considerable amount of irritation, and a large amount of hemoglobin is precipitated in the kidney tubules in the form of casts. These are so numerous that the hypothesis has been made that death is due to an intrarenal hydronephrosis — a complete blocking of the tubules with precipitated hemoglobin. I do not think that has been clearly proved, but on occasions the appearance of the kidneys suggests it.

Dr. Allen G. Brailey: Should he not have had ascites?

Dr. Mallory: It is extraordinary that he did not have it.

Dr. Hunter: Did we not have a patient eight or nine years ago in his sixties with a lipoid nephrosis?

Dr. Mallory: Yes.

Dr. Hunter: But this is not lipoid?

Dr. Mallory: No; but the symptomatology is identical. There is no way to hypothesize clinically whether the tubular degeneration is going to be of the albuminoid type or of the lipoid type.

Dr. Hunter: The interesting thing about the urinary output was that the highest was 1500 cc., when he came in, with more or less tendency downward, and he was finally putting out about 900 cc., a little more than he was taking in.

Dr. Mallory: A very high specific gravity is characteristic of the disease.

Dr. Palmer: Particularly because of the albumin?

Dr. Mallory: Yes.

CASE 25052

Presentation of Case

A fifty-seven-year-old native housewife was admitted complaining of vaginal bleeding.

She had been perfectly well, and her menses had been normal and regular until ten years before admission, at which time she had an unruptured appendix removed. The right ovary and tube were removed at the same time because, she was told, of "adhesions." Fourteen days after the operation she developed an incisional hernia. However, she had complete amenorrhea until ten months before entry when spotting with bright red blood began. Six weeks after this bleeding started she entered an outside hospital, where a left ovarian cyst and part of the ovary were removed. The pathological report was papillary cystadenoma, without evidence of carcinoma. She was discharged well in fourteen days. About a month later she began bleeding again and a series of twelve x-ray treatments was given. After another month the bleeding resumed and continued until entry. She had had no cramps, pain or weakness, though she had had occasional "dizzy and weak spells." She had lost 25 pounds in weight, from 200 to 175, during the year before entry. There were no gastrointestinal or urinary symptoms. She had had two children.

Physical examination showed an obese female in no distress. Examination of the lungs was negative. The heart was slightly enlarged to the left, and there was a rough apical systolic murmur. The sounds were regular and of good quality. The blood pressure was 205 systolic, 105 diastolic. The abdomen showed right rectus and left paramedian scars. On the right was a large incisional hernia. Vaginal examination showed a slightly enlarged uterus; there was profuse bleeding from the os. The uterus was movable. Nothing further was discovered by rectal examination.

The temperature, pulse and respirations were normal.

The urine examination showed a slight trace of albumin and 35 red cells and 20 white cells per high-power field. The blood showed a red-cell count of 2,700,000 with 55 per cent hemoglobin, and a white-cell count of 5700 with 61 per cent polymorphonuclears. The platelets were normal.

On the second hospital day an operation was performed.

Differential Diagnosis

Dr. Langdon Parsons: All this patient's trouble seems to date from her first surgical experience ten years before. One wonders about the initial diagnosis of appendicitis. There is nothing to show whether the appendix was diseased, but at any rate we go on to find that the right ovary and tube were removed. Apparently the appendix was not regarded as the sole cause of her symptoms. Whether the lesions of the tube and ovary were due to pelvic inflammation or endometriosis or anything you will, it is surprising that the other tube and ovary were not involved and likewise removed. Then after amenorrhea of ten years' duration she began to bleed bright-red blood and again entered a hospital for operation. Laparotomy was apparently done without curettage so we have no knowledge of what was going on inside the uterus. Evidently a mass was felt and proved to be ovary. The surgeon removed an ovarian cyst but only part of the ovary. There is little excuse for not removing all ovarian tissue in a woman of fifty-seven when laparotomy is done. Nothing was done about the uterus, probably for the reason that she was obese and hypertensive and regarded as a poor risk. With bleeding past the menopause, you are practically committed to do-

ing a total hysterectomy unless you can prove that there is nothing inside the uterus.

This is a controversial point and I do not know whether Dr. Meigs and Dr. Mallory will back me up, but it has been my impression that an ovarian carcinoma does not cause bleeding past the menopause unless it involves the fundus of the uterus by extension of the disease or unless it is a hormone-secreting type which produces hyperplasia of the endometrium from which bleeding occurs. If that is true, this patient was probably not bleeding because she had an ovarian cyst, and removing the cyst and part of the ovary would not be expected to end the bleeding. The original pathological specimen was reported as papillary cyst adenoma, without evidence of carcinoma. We know papillary cyst adenomas of the ovary are borderline tumors, and there may have been some portions of the tumor which were malignant, so it is conceivable that there was extension of the tumor to the uterus to account for the bleeding. However, we must go on the basis of the original pathological report, at least for the time being, and assume that it was a non-malignant tumor. If that is true, we still have not explained the bleeding. In spite of that fact, a month later x-ray treatment was given to stop the bleeding. It is my impression that x-ray treatment will not control uterine bleeding in the absence of ovarian function. In other words x-ray treatment was given without knowing why the bleeding occurred and, to my mind, with little likelihood of controlling it.

I believe the bleeding was due to a carcinoma of the fundus; as a second choice, portions of the papillary cyst adenoma might have been malignant and the bleeding may have resulted from extension of the disease to the uterine fundus.

Dr. Joe V. Meigs: To my mind the whole operative procedure was wrong. To think that a benign papillary cyst adenoma in one ovary was responsible for abnormal bleeding in a woman of fifty-seven is false reasoning. On the other hand, after looking up the cancerous lesions of the ovary in our hospital I believe some patients bleed from the endometrium who do not have extension to or hyperplasia of the endometrium. I have argued about this with Dr. Parsons for a long time. It is my impression that with certain types of ovarian tumors the endometrium may be active even though it does not show signs of hyperplasia. Some of these tumors secrete enough hormone to stimulate the endometrium, but I have also seen patients with malignancy of the ovary who bleed from apparently inactive endometrium. Why, I do not know. Hence, I do not believe it is necessary to have a metastasis or hyperplasia or even an active endometrium.

X-ray treatment should not be given to a woman fifty-seven years of age in whom a positive diagnosis as to the cause of bleeding has not been made. No one in this hospital would do it without investigating the inside of the uterus, particularly since we do not approve of x-ray treatment for postmenopausal uterine bleeding.

Dr. George G. Smith: I agree with what Dr. Meigs has said. Our experience has certainly been that it is possible to have ovarian tumors of various types, including cancer, that are associated with uterine bleeding, mostly slight in character, for which no definite cause can be found, although in some instances there is a mild degree of endometrial activity.

Clinical Diagnoses

Adenocarcinoma of uterus.
Fibroid?

Dr. Parsons's Diagnosis

Carcinoma of the fundus.
Extension of papillary adenocarcinoma of the ovary?

Anatomical Diagnoses

Adenocarcinoma of the fundus of the uterus.
Endometriosis.

Pathological Discussion

Dr. Tracy B. Mallory: On this patient's entry into the hospital a curettage was performed preliminary to hysterectomy. From a frozen section the pathologist was unable to make a definite diagnosis, though he was suspicious of carcinoma. Since he could not exclude cancer a hysterectomy was urged. The uterus was removed with considerable difficulty because it broke in the operator's hands and he had to go back and remove the cervix secondarily. The uterus therefore arrived in the laboratory in two pieces, neither of which grossly showed any obvious tumor, but on microscopical examination it is quite clear that it contains two lesions which I have not happened to see associated before. There is a frank endometrial carcinoma, and there is also a very widespread endometriosis with a considerable number of foci deep in the wall of the uterus. In some fields it is almost impossible to decide whether one is looking at endometriosis or carcinoma or perhaps a mixture of the two. In fact among the islands of endometriosis that are clearly surrounded by endometrial stroma two types of glands may be found, one of which looks fairly normal whereas the cells lining the others have all the cytologic characteristics of malignancy.

DR. PARSONS: We have seen another case in a woman of forty where the two were associated.

DR. MEIGS: Have you seen the association with any frequency, Dr. Smith?

DR. SMITH: We have had two cases with adenomyositis and carcinoma starting in the adenomyositis without endometrial involvement.

DR. MEIGS: You mean carcinoma in the wall of the endometrioma? I have never seen it.

DR. MALLORY: Here I think it is clear that the carcinoma started in the endometrium itself, not in one of the more distant spots of endometriosis. We did have one case here, I remember, where we found an adenocarcinoma in the serosa of the sigmoid with a perfectly normal mucosa and muscularis overlying it, and we raised the question whether it might not have been carcinoma starting in an endometrial implant.

DR. MEIGS: It is well known that you can have carcinoma in the ovary apparently developing from an endometrioma, but I have never happened to see it in the uterine wall. It certainly occurs in the ovarian wall and I should think you might find it in the wall of the sigmoid when an endometrioma is there. The unaccountable thing in this case is the fact that they gave x-ray treatment without knowing what was wrong inside the uterus in a woman fifty-seven years of age.

DR. MALLORY: Your inclination would be to believe that there was cancer there at that time?

DR. MEIGS: Yes, I should think so.

DR. PARSONS: Carcinomas of the fundus are slow-growing and do not take on marked activity unless they have invaded through the wall of the uterus or extended to the adnexa. A history of bleeding for a year is still consistent with carcinoma.

DR. MALLORY: It could certainly last a long period of time. I remember one case where we made a diagnosis of atypical polyp of the endometrium but, since we could not exclude cancer, advised very careful following of the patient. She was lost track of for five years, then came back, and at that time had definite cancer; but the lesion was still only 2 cm. in diameter and had not invaded the myometrium.

DR. PARSONS: Dr. Meigs has a patient known to both of us who, when told she had carcinoma of the fundus for which surgery was advised, replied: "That is interesting because I was told the same thing ten years ago and nothing was done."

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UNPRECEDENTED!

The annual New Year boasts and boosts of days gone by have ceased to concern themselves with our economic fabrics; the hoarse prophets in the market places are strangely silent. We sneak from one year to another fearfully harkening to the professional agitators and devoutly hoping that the cataclysm may be postponed another twelvemonth.

In this issue, the *Journal* presents what must be construed as the effect of society's kaleidoscopic impacts upon the health of its individuals. Somehow the bodily changes of fear, pain, hunger and rage have girded us as never before against bacterial invasions — particularly those of the respiratory tract. The death rates for tuberculosis, pneumonia and influenza have never before been so low in the United States. We do not recall that the physiologists ever made it clear that these bodily changes lead to the exercise of greater caution or prudence, but it now appears that eleven thousand fewer people were killed in accidents of all kinds (eight thousand of them having escaped deaths in automobile accidents) in the United States during 1938. Possibly this may follow the lowered sensory thresholds and consequent quicker reflex responses which would be brought about by a more or less continuous stimulation of the adrenal cortex.

When the figures are broken down there appears one sad feature; smallpox, the disease which we have known how to prevent for a hundred and forty years, was unusually prevalent in the country at large. If compulsory vaccination against smallpox cannot be contrived one must wonder how effectively compulsory health insurance can be expected to assert itself under the Stars and Stripes, preventive medicine and human nature being what they are. Even these discrepancies however may serve a useful purpose by still further stimulating our natural supplies of adrenine, and may thus bring about an even happier chart for 1939!

In all seriousness, this phenomenon must not be misinterpreted. The knowledge we have can only partially explain what is taking place. These accumulating values provide a potential bandwagon. Already we have seen them pointed to with pride by various groups. They must not be lightly interpreted, either by ourselves or others.

TULAREMIA

Tularemia is not a major health problem in the United States, but the subject is interesting inasmuch as the majority of cases can be prevented by reasonable precautions. According to Dr. A. M. Stimson, in a release from the United States Public Health Service dated December 23, 1938, totals of 8000 cases and 396 deaths had been reported up to 1938; furthermore, 613 cases had been recorded in 1938 up to November 1, not including the figures from Illinois, Ohio, Virginia and Kentucky where, for the past twelve years, high incidences have occurred.

New England has been singularly free from the disease. As pointed out elsewhere in this issue of the *Journal,* only 4 cases have been recorded, —

1 each in Rhode Island, Massachusetts, Vermont and Maine, — the present case being the fifth in New England and the second in Massachusetts. It has been pointed out in a previous editorial* that the advisability of importing Western rabbits for restocking the depleted native rabbit population is open to serious question. It is true that such a practice has apparently not resulted in the infection of native rabbits in states, such as Connecticut and New York, where restocking has been carried out for several years. This and the absence of the spontaneously occurring disease in native rabbits may be explained by a low incidence of insect vectors — ticks, lice and fleas — in most sections of the northeastern states. The climatological conditions on Cape Cod are quite different, — closely approaching those in states, such as Maryland, where tularemia is of common occurrence, — and it is not unreasonable to predict that the introduction of Western rabbits there may eventually lead to a sharply localized area where the disease in rabbits and human beings is prevalent.

The prevention of tularemia is largely a matter of personal precaution. Sick or dead wild rabbits should not be handled. Rubber gloves should be worn by those who dress them and other wild animals, but even then, sharp fragments of bone can pierce the glove and puncture the hand. Tick bites in an infested area are potentially dangerous. Rabbit meat should be thoroughly cooked. If subsequent cases of tularemia are reported from Cape Cod, instructions as to the symptoms and methods of prevention of the disease must be widely publicized.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY†

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

POSTPARTUM HEMORRHAGE

Mrs. E. C., a twenty-four-year-old primipara at term, was admitted to the hospital on June 30, 1928, after the membranes had spontaneously ruptured. She was not in labor.

Her past history was essentially negative. Catamenia began at thirteen, were regular with a twenty-eight-day cycle, and lasted four days without pain. Her last period was October 1, 1927, making her expected date of confinement July 10.

She was first seen on May 8. Physical examination showed the heart not enlarged, and the sounds regular and of good quality. The lungs were clear and resonant; there were no rales. Her blood pressure was 124 systolic, 62 diastolic. The fundus was 27 cm. above the symphysis. Vaginal examination showed the cervix soft, the vertex presenting. Her pregnancy progressed normally until entry to the hospital.

On July 2, two days after the membranes had ruptured, she was given castor oil and quinine, which resulted in pains off and on during the day. At 10 p. m. the pains were coming every five minutes and she was given chloral and morphine, which quieted her down. On July 3 a rectal examination at 8 a. m. showed the head engaged and the cervix taken up and admitting one finger. At 2 p. m. the cervix admitted three fingers, but the pains were inconsequential. Soon after this she was etherized, and a vaginal examination made. The cervix was found to admit four fingers and was soft; the fetus was in an OLA position. A version was done without difficulty, and a male child weighing 6 pounds, 9 ounces, was delivered. A minor laceration was repaired routinely. The placenta was almost immediately expressed intact, with membranes complete.

Following the delivery of the placenta, there was a great deal of fresh blood and a large clot. The uterus remained contracted for about an hour and then relaxed. With each subsequent contraction there was considerable hemorrhage. Whereas at the end of the delivery her pulse was 100, it gradually rose to 130; her blood pressure went down to 60 systolic. She was somewhat pale and perspired freely. Oxytocics were given intramuscularly without benefit. (The use of intravenous injections of pituitary extract had at that time not become general.) Her blood was matched with that of her husband, and as he was compatible, she was transfused with 600 cc., followed by 400 cc. of saline. Her pulse came down to 110; her blood pressure rose to 98 systolic, and her general condition improved. The convalescence was uneventful, and she was discharged seventeen days following delivery.

Comment. This case occurred ten and a half years ago. At that time it was a common but not

*Editorial. Tularemia. New Eng. J. Med. 216:764, 1937.

†A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

universal practice to introduce a bag if labor did not follow rupture of the membranes within twenty-four hours. In this case it was not done. Today, when it is known that there is no pelvic disproportion, most men are indifferent to the early rupture of the membranes, because experience has taught that the great majority of such cases will start in satisfactory labor even if there is a delay of three to five days before the onset of labor. Occasionally such an occurrence does result in a prolonged, unsatisfactory labor, and any such patient may experience postpartum hemorrhage.

Version was done in this case because the head was not low, the cervix was not completely dilated, and satisfactory progress was not being made. The operation of version in primiparas must always be undertaken with an appreciation of its inherent dangers and should not be performed by one poorly trained in the art of obstetrics.

Apparently the placenta separated very soon after the birth of the baby and may have been partially separated before the baby was born. Evidence of this was the large clot and unusual amount of fresh bleeding which immediately followed the delivery of the placenta.

The periods of relaxation in this uterus were much longer than those of contraction, and there was apparently considerable bleeding during the former, which resulted in the loss of more blood than was normal. Transfusion not only replaced lost blood but, as so often happens, stimulated the uterus to contract. Neither the amount of bleeding nor the condition of the uterus made packing necessary. The excellent result following transfusion proved this to have been the correct procedure.

LEGISLATIVE NOTES

The following bills before the Legislature are scheduled for a public hearing before the Committee on Public Health on February 9:

SENATE 258. Bill relative to the meaning of the terms "rendering medical service," "practice of medicine," et cetera.

HOUSE 59. Same as S. 258.

HOUSE 60. Bill relative to the annual registration of physicians.

HOUSE 985. Bill relative to doctors of medicine and doctors of osteopathy on the Board of Registration in Medicine.

HOUSE 986. Bill relative to a doctor of medicine and a doctor of osteopathy on the Approving Authority.

POSTGRADUATE EXTENSION COURSES

The programs of instruction to be given this spring by the Massachusetts Medical Society in cooperation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau are listed below. These courses are offered free to all legally registered physicians in Massachusetts.

BARNSTABLE DISTRICT

Place: HYANNIS

SUBJECT	DATE
Bleeding in the Third Trimester of Pregnancy	March 5
Heart Disease: The treatment of "heart attacks" or "cardiovascular emergencies"	March 12
Syphilis: Latent syphilis — diagnosis and treatment	March 19
Gonorrhea: Modern treatment of gonorrhea	March 26
Cesarean Section; Analgesia	April 2
The Indications and Contraindications for Removal of Tonsils and Adenoids	April 9
Anemia: Modern methods in diagnosis and treatment of blood dyscrasias	April 16
Bright's Disease and Hypertension: Evaluation of new therapy; diagnosis	April 23

Meetings to be held at the Cape Cod Hospital, Sundays, at 4:00 p. m.

Donald E. Higgins, M.D., *Chairman.*

BERKSHIRE DISTRICT

Place: PITTSFIELD

SUBJECT	DATE
Bright's Disease and Hypertension: Evaluation of new therapy; diagnosis	March 9
Anemia: Modern methods in diagnosis and treatment of blood dyscrasias	March 16
Sepsis	March 23
Syphilis: Latent syphilis — diagnosis and treatment	March 30
Gonorrhea: Modern treatment of gonorrhea	April 6
Heart Disease: The treatment of "heart attacks" or "cardiovascular emergencies"	April 13
The Indications and Contraindications for Removal of Tonsils and Adenoids	April 20
The Control and Treatment of Respiratory Infections. (This is to include the serological treatment of pneumonia in infants and children.)	April 27

Meetings to be held at the House of Mercy Hospital, Thursdays, at 4:30 p. m.

Melvin H. Walker, Jr., M.D., *Chairman.*

BRISTOL NORTH DISTRICT

Place: TAUNTON

SUBJECT	DATE
Anemia: Modern methods in diagnosis and treatment of blood dyscrasias	February 9
Bright's Disease and Hypertension: Evaluation of new therapy; diagnosis	February 16

Heart Disease: The treatment of "heart attacks" or "cardiovascular emergencies" ..... February 23
Operative Obstetrics ..... March 2
The Control and Treatment of Respiratory Infections. (This is to include the serological treatment of pneumonia in infants and children.) ..... March 9
Gonorrhea: Modern treatment of gonorrhea ..... March 16
Syphilis: Latent syphilis — diagnosis and treatment ..... March 23
Bleeding in the Third Trimester of Pregnancy ..... March 30

Meetings to be held at the Morton Hospital, Thursdays, at 4:00 p. m.

Lester E. Butler, M.D., *Chairman.*

Bristol South District

Place: FALL RIVER

SUBJECT	DATE
Gonorrhea: Modern treatment of gonorrhea	February 7
Syphilis: Latent syphilis — diagnosis and treatment	February 14
Medical Complications in Pregnancy	February 21
Whooping Cough: The present status of vaccine therapy, both as prophylactic and therapeutic measures; the early diagnosis by laboratory procedures; and the treatment of complications	February 28
Anemia: Modern methods in diagnosis and treatment of blood dyscrasias	March 7
Bright's Disease and Hypertension: Evaluation of new therapy; diagnosis	March 14
Heart Disease: The treatment of "heart attacks" or "cardiovascular emergencies"	March 21
The Control and Treatment of Respiratory Infections. (This is to include the serological treatment of pneumonia in infants and children.)	March 28

Meetings to be held at the Union Hospital, Tuesdays, at 4:00 p. m.

Howard P. Sawyer, M.D.,
Robert H. Goodwin, M.D.,
Chairmen.

Franklin District

Place: GREENFIELD

SUBJECT	DATE
Heart Disease: The treatment of "heart attacks" or "cardiovascular emergencies"	March 8
Bleeding in the Third Trimester of Pregnancy	March 15
Whooping Cough: The present status of vaccine therapy both as prophylactic and therapeutic measure; the early diagnosis by laboratory procedures; and the treatment of complications	March 22
Bright's Disease and Hypertension: Evaluation of new therapy; diagnosis	March 29
Sepsis	April 5
Syphilis: Latent syphilis — diagnosis and treatment	April 12
Gonorrhea: Modern treatment of gonorrhea	April 26
Anemia: Modern methods in diagnosis and treatment of blood dyscrasias	May 3

Meetings to be held at the Franklin County Public Hospital, Wednesdays, at 8:00 p. m.

Halbert G. Stetson, M.D., *Chairman.*

Note: Because of the holiday, the course will be omitted April 19.

Hampden District

Places: SPRINGFIELD, HOLYOKE

SUBJECT	DATE
Anemia: Modern methods in diagnosis and treatment of blood dyscrasias	March 2
Heart Disease: The treatment of "heart attacks" or "cardiovascular emergencies"	March 9
Syphilis: Latent syphilis — diagnosis and treatment	March 16
Gonorrhea: Modern treatment of gonorrhea	March 23
The Indications and Contraindications for Removal of Tonsils and Adenoids	March 30
Bright's Disease and Hypertension: Evaluation of new therapy; diagnosis	April 6
Bleeding in the Third Trimester of Pregnancy	April 13
The Control and Treatment of Respiratory Infections. (This is to include the serological treatment of pneumonia in infants and children.)	April 20

Meetings to be held Thursdays at the Academy of Medicine, Professional Building, 20 Maple Street, Springfield, at 4:00 p. m., and in the Outpatient Department of the Skinner Clinic, Holyoke Hospital, Holyoke, at 8:00 p. m.

George L. Schadt, M.D., *Chairman.*

Middlesex East District

Place: MELROSE

SUBJECT	DATE
Medical Complications in Pregnancy	February 7
Whooping Cough: The present status of vaccine therapy, both as prophylactic and therapeutic measures; the early diagnosis by laboratory procedures; and the treatment of complications	February 14
The Indications and Contraindications for Removal of Tonsils and Adenoids	February 21
Bright's Disease and Hypertension: Evaluation of new therapy; diagnosis	February 28
Gonorrhea: Modern treatment of gonorrhea	March 7
Syphilis: Latent syphilis — diagnosis and treatment	March 14
Anemia: Modern methods in diagnosis and treatment of blood dyscrasias	March 21
Heart Disease: The treatment of "heart attacks" or "cardiovascular emergencies"	March 28

Meetings to be held at the Melrose Hospital (Colby Hall), Tuesdays, at 4:00 p. m.

Walter H. Flanders, M.D., *Chairman.*

MIDDLESEX NORTH DISTRICT

Place: LOWELL

SUBJECT	DATE
The Indications and Contraindications for Removal of Tonsils and Adenoids	February 9
Gonorrhea: Modern treatment of gonorrhea	February 16
Syphilis: Latent syphilis — diagnosis and treatment	February 23
Heart Disease: The treatment of "heart attacks" or "cardiovascular emergencies"	March 2
Delivery and the Puerperium	March 9
The Toxemias of Pregnancy	March 16
Bright's Disease and Hypertension: Evaluation of new therapy; diagnosis	March 23
Anemia: Modern methods in diagnosis and treatment of blood dyscrasias	March 30

Meetings to be held at St. John's Hospital, Thursdays, at 4:30 p. m.

William S. Lawler, M.D., *Chairman.*

MIDDLESEX SOUTH DISTRICT

Place: CAMBRIDGE

SUBJECT	DATE
Bright's Disease and Hypertension: Evaluation of new therapy; diagnosis	March 7
Anemia: Modern methods in diagnosis and treatment of blood dyscrasias	March 14
Heart Disease: The treatment of "heart attacks" or "cardiovascular emergencies"	March 21
Medical Complications in Pregnancy	March 28
Whooping Cough: The present status of vaccine therapy both as prophylactic and therapeutic measures; the early diagnosis by laboratory procedures; and the treatment of complications	April 4
Operative Obstetrics	April 11
Gonorrhea: Modern treatment of gonorrhea	April 18
Syphilis: Latent syphilis — diagnosis and treatment	April 25

Meetings to be held at the Cambridge Hospital, 330 Mt. Auburn Street, Tuesdays, at 5:00 p. m.

Alexander A. Levi, M.D., *Chairman.*

* * *

FACULTY

Anemia. Chairman: Dr. William P. Murphy. Instructors: Drs. Greene FitzHugh, Clark W. Heath, Chester S. Keefer, George R. Minot and Maurice B. Strauss.

Bright's Disease and Hypertension. Chairman: Dr. James P. O'Hare. Instructors: Drs. Laurence B. Ellis, W. Richard Ohler and Robert S. Palmer.

Heart Disease. Chairman: Dr. Paul D. White. Instructors: Drs. Edward F. Bland, Francis L. Chamberlain, Wilfrid J. Comeau, Marshall N. Fulton, R. Earle Glendy, Ashton Graybiel, Burton E. Hamilton, T. Duckett Jones, Samuel A. Levine, Benedict F. Massell, Sylvester McGinn, Joseph H. Pratt, William D. Reid, Howard B. Sprague and Oliver H. Stansfield.

Gonorrhea. Chairman: Dr. E. Granville Crabtree. Instructors: Drs. Weston T. Buddington, Fletcher H. Colby, Oscar F. Cox, Jr., Roger C. Graves, Sylvester B. Kelley, George C. Prather and Samuel N. Vose.

Syphilis. Chairman: Dr. E. Granville Crabtree. Instructors: Drs. William P. Boardman, Rudolph Jacoby, C. Guy Lane and Francis M. Thurmon.

Obstetrics. Chairman: Dr. Robert L. DeNormandie. Instructors: Drs. De Los J. Bristol, Jr., Christopher J. Duncan, M. Fletcher Eades, A. Gordon Gauld, Thomas R. Goethals, Roy J. Heffernan, James C. Janney, M. V. Kappius, Foster S. Kellogg, Joseph W. O'Connor, John Rock, Judson A. Smith and Raymond S. Titus.

Pediatrics. Chairman: Dr. Warren R. Sisson. Instructors: Drs. James M. Baty, Allan M. Butler, Stewart H. Clifford, John Davies, Louis K. Diamond, R. Cannon Eley, Carlyle G. Flake, Joseph Garland, Harold L. Higgins, Charles I. Johnson, Charles F. McKhann, Edwin H. Place, Clement A. Smith and Edwin T. Wyman.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions, given by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau, have been arranged for the week beginning February 6:

BRISTOL NORTH

Thursday, February 9, at 4:00 p. m., at the Morton Hospital, Taunton. Subject — Anemia: Modern methods in diagnosis and treatment of blood dyscrasias. Instructor: Maurice B. Strauss. Lester E. Butler, *Chairman.*

BRISTOL SOUTH (Fall River Section)

Tuesday, February 7, at 4:00 p. m., at the Union Hospital, Fall River. Subject — Gonorrhea: Modern treatment of gonorrhea. Instructor: Oscar F. Cox, Jr. Howard P. Sawyer, *Chairman.*

MIDDLESEX EAST

Tuesday, February 7, at 4:00 p. m., at the Melrose Hospital (Colby Hall), Melrose. Subject — Medical Complications in Pregnancy. Instructor: James C. Janney. Walter H. Flanders, *Chairman.*

MIDDLESEX NORTH

Thursday, February 9, at 4:30 p. m., at St. John's Hospital, Lowell. Subject — The Indications and Contraindications for Removal of Tonsils and Adenoids. Instructor: Warren R. Sisson. William S. Lawler, *Chairman.*

DEATHS

CLARK — GEORGE S. CLARK, M.D., of 12 Germain Street, Worcester, died January 27. He was in his eightieth year.

Born in Hardwick, he graduated from Hitchcock Free High School and taught school for several years. He received his degree from the Harvard Medical School in 1885. Dr. Clark was a member of the American Medical Association and the Massachusetts Medical Society and had practiced medicine in Worcester for fifty-seven years.

His widow, four daughters, a sister and two brothers survive him.

EMERY — WILLIAM H. EMERY, M.D., of 109 Warwick Street, Roxbury, died January 21. He was in his ninety-first year.

Dr. Emery received his degree from the Harvard Medical School in 1870 and, in his younger days, was an associate of Dr. Oliver W. Holmes.

He was a member of the Massachusetts Medical Society and the American Medical Association.

FERNALD — GUY G. FERNALD, M.D., of Elm Street, West Concord, died January 26. He was in his seventy-fifth year.

Born in Wilton, Maine, he attended Wilton Academy, State Normal School, St. Johnsbury Academy and Dartmouth College and, in 1899, received his degree from the Dartmouth Medical School. He served his internship at Mary Hitchcock Memorial Hospital, Hanover, New Hampshire, and then joined the staff of the McLean Hospital at Waverley. In 1908 he went to the Massachusetts Reformatory Hospital at West Concord where he remained for twenty-seven years. Dr. Fernald served as principal in the boys' division at the Perkins Institute for the Blind, disciplinarian at Friends' School, Providence, and while at the reformatory organized the psychopathological laboratory.

He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a son and two brothers survive him.

SEGUR — WILLARD B. SEGUR, M.D., of Enfield, died January 27. He was in his seventy-fourth year.

Dr. Segur graduated from Phillips Andover Academy and Princeton University, and received his degree from Dartmouth Medical School in 1892. For many years he practiced medicine in the Quabbin Valley area and had been medical examiner of the fourth Hampshire district for the past twenty years.

He was a fellow of the American Medical Association and of the Massachusetts Medical Society.

His widow and a son survive him.

WOODWARD — LEROY A. WOODWARD, M.D., of 5 High Street, Worcester, died January 22. He was in his fifty-fifth year.

Dr. Woodward attended the public schools in Pawtucket, Rhode Island, and later entered the Rhode Island College of Pharmacy, graduating in 1906. He graduated from Tufts College Medical School in 1914 and interned at the House of Mercy Hospital, Pittsfield, and the Worcester City Hospital. He was chief surgeon at the Harvard Private Hospital, Worcester.

He was a fellow of the Massachusetts Medical Society and the American Medical Association.

MISCELLANY

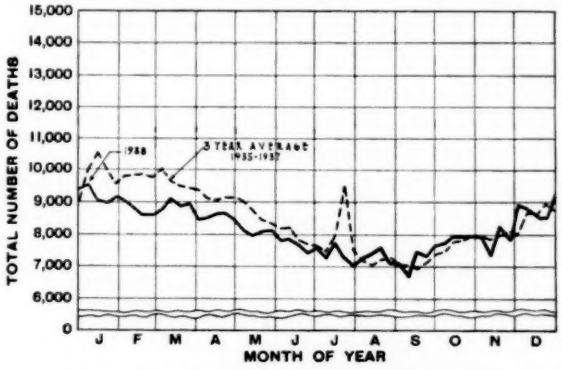
ANNUAL MORTALITY SUMMARY FOR 1938

Deaths in eighty-eight major cities during 1938 were 6 per cent under the 1937 figures, according to preliminary reports recently made public by Director William L. Austin, of the Bureau of the Census, Department of Commerce. The infant death rate in these cities was also slightly lower last year, compared with 1937.

Deaths in the eighty-eight cities in 1938 totaled 424,189 compared with 449,555 reported for 1937, which is a decrease of 5.6 per cent. The provisional infant mortality rate for the eighty-eight cities is 43 per 1000 live births, compared with 47 in 1937.

The weekly death totals reported in 1938 were consistently lower than the average totals for the preceding three years from January to July, inclusive. During the rest of the year, however, the 1938 weekly totals were closely similar to the averages of the preceding three years.

The more favorable mortality record of 1938 as compared with the average of the preceding three years is due, probably, to the smaller number of deaths from influenza and pneumonia during the winter and to the less extreme heat conditions during the summer.



Total Deaths by Weeks in Eighty-Eight Major Cities of the United States.

The 27,147 infant deaths reported for 1938 represent a decrease of 1598, or 5.6 per cent, from the 28,745 reported for 1937. On the basis of estimated number of births, there were, in 1938, 43 infant deaths for each 1000 births. Although this figure is provisional, it indicates a real decrease in infant mortality when compared with the comparable provisional rate of 47 for 1937.

In the comparison of infant rates for different cities, certain considerations must not be overlooked. Primarily, the effect of differences in sex, age and racial composition of different cities must be evaluated before valid comparisons can be made.

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR NOVEMBER, 1938

DISEASES	NOV. 1938	NOV. 1937	FIVE-YEAR AVERAGE*
Anterior poliomyelitis	0	6	16
Chickenpox	811	973	976
Diphtheria	21	8	43
Dog bite	666	598	540
Dysentery, bacillary	9	37	68
German measles	30	39	61
Gonorrhea	421	589	544
Lobar pneumonia	233	269	300
Measles	597	282	482
Meningococcus meningitis	2	5	5
Mumps	257	266	347
Paratyphoid B fever	12	6	2
Scarlet fever	356	594	627
Syphilis	503	558	453
Tuberculosis, pulmonary	262	225	266
Tuberculosis, other forms	30	24	28
Typhoid fever	6	15	8
Undulant fever	5	2	3
Whooping cough	558	471	758

*Based on figures for preceding five years.

RARE DISEASES

Anthrax was reported from: Somerville, 1; total, 1.

Diphtheria was reported from: Boston, 1; Burlington, 1; Cambridge, 1; Gloucester, 1; Groveland, 1; Fall River, 3; Lawrence, 10; Medford, 1; Methuen, 1; North Andover, 1; total, 21.

Dysentery, bacillary was reported from: Amherst, 1;

Beverly, 1; Boston, 2; Danvers, 1; Lowell, 1; New Bedford, 1; Norwood, 1; West Springfield, 1; total 9.

Infectious encephalitis was reported from: Chelmsford, 1; Chelsea, 1; Foxboro, 1; Middleboro, 1; total, 4.

Meningococcus meningitis was reported from: Marblehead, 1; West Townsend, 1; total, 2.

Paratyphoid B fever was reported from: Lynn, 4; Medford, 1; Springfield, 2; Wellesley, 1; West Bridgewater, 3; Williamsburg, 1; total, 12.

Pellagra was reported from: Revere, 1; total, 1.

Septic sore throat was reported from: Boston, 5; Lawrence, 3; Marblehead, 1; Woburn, 1; total, 10.

Trachoma was reported from: Boston, 1; Fitchburg, 1; Worcester, 1; total, 3.

Trichinosis was reported from: Boston, 1; Fall River, 1; total, 2.

Typhoid fever was reported from: Boston, 1; Chelsea, 1; Holyoke, 1; Ludlow, 3; total, 6.

Undulant fever was reported from: Boston, 1; Brockton, 1; Dalton, 1; Fitchburg, 1; Millbury, 1, total, 5.

Anterior poliomyelitis showed record low incidence. Measles and tuberculosis (other forms) were reported above the five-year average.

Lobar pneumonia, pulmonary tuberculosis, mumps and diphtheria were reported below the five-year average. Meningococcus meningitis showed record low figures except for the years 1925 and 1934 which were equaled. Chickenpox, German measles and scarlet fever were reported below the five-year average. Undulant fever showed record high figures except for the year 1936 which was equaled. Paratyphoid B fever was reported at a record high figure.

Animal rabies continued to show low incidence. New foci were noted in Newbury and Haverhill.

"YOUR HEALTH" BROADCASTS

The next series of "Your Health" broadcasts, sponsored by the American Medical Association and the National Broadcasting Company and heard over the Blue Network each Wednesday at 2:00 p. m., is entitled "Health for Tomorrow." It consists of four broadcasts as follows:

February 8. Avoiding Arthritis.
Known factors in the causation of arthritis; its care.

February 15. Healthy Hearts.
Known ways of protecting the heart against infection and hygienic abuse; how to live with heart disease.

February 22. Cancer Can Be Cured.
Known factors in the cause, prevention and treatment of cancer.

March 1. Diabetes.
Individual efforts plus medical aid win against diabetes.

CORRESPONDENCE

AN ADVOCATE OF SOCIALIZED MEDICINE

To the Editor: The medical profession faces a serious situation, a menace to the very existence of the doctor. The menace consists in the disorganized and disappearing practice of the doctors. This is partly caused, partly aggravated, by commercial competition of private clinics, hospitals, dispensaries, sanatoriums, medical centers, foundations, insurance and industrial medical departments, teaching clinics and hospitals, lodge and contract practice, federal, state and municipal public-health departments, city hospitals, state-favored private medical services and organizations, physicians holding more than one paying position, not to mention all the various cults, commercial quackery, counter-prescribing by druggists, self-treatment and, last but not least, a poor and inadequate social service to investigate each case which applies for free treatment.

The doctor cannot solve his problem by evading the issue or romancing about it. He must face the realities of economic and medical life. The prevailing general economic conditions of depression have still more accentuated the sad state of the doctor. The doctor must organize properly to meet conditions as they now exist with his fellows and, if need be, apply liberal or even radical remedies, because the powers to be of the American Medical Association together with those physicians holding key positions, fear the loss of their prestige and therefore are not interested, or at least do not show it, taking in consideration what they say and even write with their pens, to help the physician and see to it that no physician is starving. I might say here that there are many physicians, yes thousands or more, who find it very difficult to pay rent, forgetting about meeting the ordinary everyday necessities of life, due to no fault of their own but for causes as stated before. The day of so-called "rugged individualism" is gone forever and has left "ragged individuals."

Thousands of persons, or to be exact, as our able and efficient Surgeon General of United States, Thomas Parran, said in his annual report, 40,000,000 people in the United States, the lower economic third of our population, are unable to provide themselves with medical care during serious illness, and the country is short 360,000 hospital beds. Many people are ashamed to ask for free medical care, others can only afford to pay a small fee, others cannot pay what they feel the physician should get, therefore they all lack medical care.

Private competitive practice is an anachronism and a failure, because the private physician cannot compete with the aforementioned causes and must gradually die by the wayside.

Unless and until the practice of medicine returns to where it rightfully belongs, namely to the private practicing physician, and before such is possible, all hospital plans over the country must be abolished, and all abuses in our hospitals, outpatient departments, and so forth, must meet the same ordeal together with what I have already set forth in my first paragraph, and by so doing the physician can again begin earning a living, then only would the medical economic upset subside. After carefully observing, for the past ten years, the gradual loss of more and more private medical practice, there is only one salvation, and that is the acceptance by the medical profession as a whole the help by the federal government under specific rules and regulations and pay each and every physician who is willing, and God only knows more than a majority of the physicians are willing, to be paid a stipulated reasonable salary and the physicians in turn will treat the needy individuals.

The federal government has already undertaken to spend $850,000,000 and that sum will be increased depending on conditions. To give you one specific instance, $3,000,000 was appropriated for venereal control, and now Dr. Parran is requesting the sum be increased gradually to $25,000,000 a year.

If the medical profession will not give immediate consideration to what the federal government has already pledged itself to do, namely a square and fair deal to the

backbone of the medical profession ("general practitioners"), and not play with time, by waiting to see what may or will result in the pending government's case for alleged violation of antitrust laws against the American Medical Association and against others, organized medicine will treat its colleagues to a total economic disaster. The doctors should and must have a clear and true understanding of the real situation that is facing them, a realization of the actual causes and the logical cure of this present serious condition. Do not stand on the side lines and be unconcerned because you are earning a living. Unite; give a helping hand to all members of the medical profession, because many of them are worse off than those who apply for medical aid!

Practically all articles printed in our medical journals have never to date stated the actual true facts, but they have always clouded the real issues. The medical profession must awake from its lethargy, or accept defeat.

BERNARD ZUCKERMAN, M.D.

978 Blue Hill Avenue,
Dorchester, Mass.

APPOINTMENT TO BOARD OF REGISTRATION IN MEDICINE

To the Editor: This is to inform you that Dr. Dominzio A. Costa, 261 Hanover Street, Boston, having been appointed by former Governor Hurley as a member of the Board of Registration in Medicine, qualified on December 16, 1938.

STEPHEN RUSHMORE, M.D., *Secretary.*

Board of Registration in Medicine,
State House, Boston.

According to statutory requirements, it was necessary for Dr. Costa to resign from the Massachusetts Medical Society to become eligible for appointment to the Board. ED.

REPORTS OF MEETINGS

MEETING IN HONOR OF PRESIDENT CARMICHAEL

A Tufts College Medical School faculty meeting in honor of President Leonard Carmichael, of Tufts College, was held Wednesday, February 1, at 6:30 p. m., at the Algonquin Club in Boston.

A pageant, depicting medical affairs at the time of the founding of the School in 1893, and during its first few years, was one of the features of the evening.

A. Warren Stearns, M.D., dean of the medical school, was chairman of the dinner arrangements and was assisted by Louis E. Phaneuf, M.D., professor of gynecology; Benjamin Spector, M.D., professor of anatomy, directed the pageant.

EASTERN HAMPDEN MEDICAL ASSOCIATION

The stated monthly meeting of the Eastern Hampden Medical Association was held on January 12 at the Oaks Hotel in Springfield.

The paper of the evening, entitled "Some Common Mistakes," was presented by Dr. Erdix T. Smith, of Springfield. He pointed out some commonly made errors in diagnosis and treatment and especially decried the handling of fracture cases by some of the younger men with inadequate training along these lines. He suggested that a competent consultant should be called in order to avoid protracted and permanent disability in these cases.

A general discussion of the paper followed, led by Dr. Richard E. Dickson, of Holyoke.

J. JOSEPH KLAR, M.D., *Secretary.*

NOTICES

REMOVAL

W. FENN HOYT, M.D., announces the removal of his office to 11 High Street, Springfield.

ANNOUNCEMENT

WILLIAM K. NANCE, M.D., who for the past two years has been a member of the resident staff of the Ring Sanatorium and Hospital, has opened an office at 7 Park Circle, Arlington Heights. Associated with him is Doris Hoffman, M.D.

JOHN T. BOTTOMLEY SOCIETY

The next meeting of the John T. Bottomley Society will be held in the Out-Patient Department of the Carney Hospital on Tuesday, February 7, at 11:30 a. m.

PROGRAM

Care of the Feet in Diabetes. Dr. George Cleary.
Advantages and Disadvantages of Protamine Insulin. Dr. Charles Finnerty.

WILLIAM J. MACDONALD, M.D., *Secretary.*

BOSTON CITY HOSPITAL

The monthly clinicopathological conference will be held at the Boston City Hospital on Wednesday, February 8, at 12 o'clock noon, in the Pathological Amphitheater.

JOSEPH E. HALLISEY, M.D., *Secretary,*
Medical Staff.

NEW ENGLAND DERMATOLOGICAL SOCIETY

The next meeting of the New England Dermatological Society will be held on Wednesday, February 8, at 2:00 p. m., in the Skin Out Patient Department of the Massachusetts General Hospital. Following the clinical meeting, dinner will be served at the Hotel Kenmore.

The guest speaker at the dinner will be Dr. E. William Abramowitz, associate professor of dermatology and syphilology at the New York Post-Graduate Medical School, Columbia University. The subject will be "Remarks on the Action of Certain Drugs in the Local and General Treatment of Various Dermatoses."

Reservations for the dinner should be made with the secretary.

BERNARD APPEL, M.D., *Secretary.*

GREATER BOSTON MEDICAL SOCIETY

There will be a meeting of the Greater Boston Medical Society at the Beth Israel Hospital on Tuesday evening, February 7, at 8:15.

Dr. Soma Weiss will speak on "Etiological Factors and Therapeutic Measures in Circulatory Collapse and Shock." Discussion by Drs. Herrman L. Blumgart, Charles G. Mixter and Jacob Fine will follow.

LOUIS M. FREEDMAN, M.D., *President,*
DAVID B. STEARNS, M.D., *Secretary.*

WEST ROXBURY MEDICAL ASSOCIATION

A meeting of the West Roxbury Medical Association will be held in Highland Hall, 1868 Centre Street, West Roxbury, on Tuesday, February 7, at 8:30 p. m.

SYMPOSIUM ON HEADACHE

Eyes. Dr. Benjamin Sachs.
Nose and Throat. Dr. Josiah Quincy.
General Medicine. Dr. Norman Welch.
Neurological Aspects. Dr. Maxwell MacDonald.

Collation.

DAVID L. LIONBERGER, M.D., *Secretary.*

UROLOGICAL CONFERENCE

A urological conference will be held at 12 o'clock noon on the first and third Fridays of February, March, April and May in the Lower Out-Patient Amphitheater of the Massachusetts General Hospital.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, INCORPORATED

The general oral, clinical and pathological examinations for all candidates, Part 2 examinations (Groups A and B), will be conducted by the entire board, meeting in St. Louis, Missouri, on May 15 and 16, immediately prior to the annual meeting of the American Medical Association. Notice of time and place of these examinations will be forwarded to all candidates well in advance of the examination dates.

Candidates for re-examination in Part 2 (Groups A and B) must request such re-examination by writing the secretary's office before April 1. Candidates who are required to take re-examinations must do so before the expiration of three years from the date of their first examination.

The annual dinner meeting of the board, to which all diplomates and candidates are invited, as well as their wives and others interested in the work of the board, will be held at the Congress Hotel, St. Louis, on Wednesday evening, May 17, following the close of the examinations.

Application for admission to the Group A examinations must be on file in the secretary's office not later than March 15. Application blanks and booklets of information may be obtained from Dr. Paul Titus, secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

TUMOR CLINIC, BOSTON DISPENSARY

Each Tuesday and Friday morning, 10:00 to 12:30, there is a meeting of the Tumor Clinic of the Boston Dispensary, a unit of the New England Medical Center. Neoplasms of various sorts are seen and discussed, and when there is an indication, are treated with radium of high-voltage x-ray. Physicians are invited to visit this clinic. They may bring patients for aid in diagnosis or may refer patients to the clinic following which a report will be returned to the referring physician. A limited number of beds are available for diagnostic study and for treatment.

MEDICAL CLINIC AT THE PETER BENT BRIGHAM HOSPITAL

At 3:30 p. m. on Thursday, February 9, in the amphitheater of the Peter Bent Brigham Hospital, Dr. C. Sidney Burwell, research professor of clinical medicine and dean, Harvard Medical School and physician, Peter Bent Brigham Hospital, will give a medical clinic. Practitioners and medical students are cordially invited to attend.

TEMPERATURE SYMPOSIUM

A symposium on "Temperature and Its Measurement in Science and Industry" will be held under the auspices of the American Institute of Physics, probably next fall, the dates to be announced later. Consistent with the title, the symposium will broadly cover many fields, its primary purposes according to present plans being to (1) co-ordinate the treatment of the subject in the sciences and branches of engineering, (2) review principles and bring up to date the record of recent work, (3) accumulate contributions for a comprehensive text, to be published as soon as possible after the symposium is held, (4) reveal the subject as an important branch of physics and (5) supply schools with the information required for the improvement of curricula. The Institute confidently expects that a stimulating, valuable and unified program will be arranged, an aim which will require the help of many contributors.

A representative steering committee has been formed consisting of: the chairman, C. O. Fairchild, director of research, C. J. Tagliabue Manufacturing Co.; Dr. E. F. DuBois, medical director, Russell Sage Institute of Pathology and professor of medicine, Cornell University Medical College; Dr. Gustav Egloff, director of research, Universal Oil Products Co.; Dr. John Johnston, director of research, United States Steel Corporation; Dr. W. G. Whitman, head, Department of Chemical Engineering, Massachusetts Institute of Technology; and Dr. H. A. Barton, director, American Institute of Physics.

Those who are interested in taking part in this symposium should communicate with the Institute at an early date, giving information regarding their field of work and the subject of the contribution they wish to make. Such contributions will be co-ordinated with the subjects of a group of invited papers, and assignments and divisions made. Further information for contributors will be available shortly. Address all communications to: American Institute of Physics, 175 Fifth Avenue, New York City.

HARVARD MEDICAL SCHOOL LECTURES

The following lectures will be given in Amphitheater C of the Harvard Medical School at 5 p. m.

February 9 — Lecture on the Care of the Patient. Dr. Donald Guthrie of Sayre, Pennsylvania.

February 16 — George W. Gay Lecture on Medical Ethics. Dr. Robert L. DeNormandie.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, FEBRUARY 6

MONDAY, FEBRUARY 6

*4 p. m. Physicians and medical students are cordially invited to attend a clinic presented by the medical, surgical and orthopedic services of the Infants' and Children's hospitals, in the amphitheater of the Children's Hospital.

TUESDAY, FEBRUARY 7

*9-10 a. m. Joseph H. Pratt Diagnostic Hospital. Diagnosis of Certain Shoulder Conditions. Dr. J. D. Adams.

*10 a. m. - 12:30 p. m. Tumor clinic. Boston Dispensary.

11:30 a. m. John T. Bottomley Society. Carney Hospital.

*8 p. m. Robert B. Brigham Hospital.

8:15 p. m. Greater Boston Medical Society. Beth Israel Hospital.

WEDNESDAY, FEBRUARY 8

*9-10 a. m. Joseph H. Pratt Diagnostic Hospital. Hospital case presentation. Dr. S. J. Thannhauser.

*12 m. Clinicopathological conference. Children's Hospital Amphitheater.

12 m. Boston City Hospital. Clinicopathological conference. Pathological Amphitheater.

2 p. m. New England Dermatological Society. Massachusetts General Hospital.

THURSDAY, FEBRUARY 9

8:30-9:30 a. m. Exchange visit, Surgical and Orthopedic Staffs of the Peter Bent Brigham and Children's hospitals, held this week at the Children's Hospital Surgical.

*9-10 a. m. Joseph H. Pratt Diagnostic Hospital. The Present Status of Vitamin B. Dr. L. R. Weiss.

*3:30 p. m. Medical clinic at the Peter Bent Brigham Hospital.

5 p. m. Lecture on the Care of the Patient. Harvard Medical School, Amphitheater C.

FRIDAY, FEBRUARY 10

*9-10 a. m. Joseph H. Pratt Diagnostic Hospital. Recent Studies on Gout. Dr. J. H. Talbott.

*10 a. m. - 12:30 p. m. Tumor clinic. Boston Dispensary.

SATURDAY, FEBRUARY 11

*9-10 a. m. Joseph H. Pratt Diagnostic Hospital. Hospital case presentation. Dr. S. J. Thannhauser.

*10 a. m. - 12 m. Staff rounds of the Peter Bent Brigham Hospital. Conducted by Dr. Henry A. Christian.

SUNDAY, FEBRUARY 12

4 p. m. Illustrated, public, health lecture, Faulkner Hospital, auditorium. Surgical Diseases of the Liver and the Bile Passages. Dr. Franklin G. Balch, Jr.

4 p. m. Free public lecture, Harvard Medical School, Amphitheater of Building D. Asthma and Hay Fever. Dr. Henry N. Pratt.

*Open to the medical profession.

FEBRUARY 3 — Urological Conference. Massachusetts General Hospital. Page 218.

FEBRUARY 5 — Lecture at the Faulkner Hospital. Page 971, issue of December 15.

FEBRUARY 5 — Free Public Lecture, Harvard Medical School. Page 1056, issue of December 29.

FEBRUARY 5 — Beverly Hospital Public Health Lecture. Page 1056, issue of December 29.

FEBRUARY 5 — Salem Hospital Public Health Lecture. Page 126, issue of January 19.

FEBRUARY 7 — John T. Bottomley Society. Page 217.

FEBRUARY 7 — Lawrence Cancer Clinic. Page 173, issue of January 26.

FEBRUARY 7 — Robert B. Brigham Hospital. Page 125, issue of January 19.

FEBRUARY 7 — Greater Boston Medical Society. Page 217.

FEBRUARY 7 — West Roxbury Medical Association. Page 217.

FEBRUARY 8 — Boston City Hospital. Clinicopathological Conference. Page 217.

FEBRUARY 8 — New England Dermatological Society. Page 217.

FEBRUARY 9 — Medical Clinic, Peter Bent Brigham Hospital. Page 218.

FEBRUARY 9 — Lecture on the Care of the Patient. Page 218.

FEBRUARY 9 — Pentucket Association of Physicians, 8:30 p. m., Hotel Bartlett, 95 Main Street, Haverhill.

FEBRUARY 16 — George W. Gay Lecture on Medical Ethics. Page 218.

FEBRUARY 17 — Urological Conference. Massachusetts General Hospital.

FEBRUARY 22 — Alumni Day, New York University College of Medicine. Page 173, issue of January 26.

MARCH 13 — Fourth Annual Postgraduate Institute. Page 938, issue of December 8.

MARCH 15, MAY 15, AUGUST 5 and OCTOBER 6 — American Board of Ophthalmology. Page 126, issue of January 19.

MARCH 27-31 — American College of Physicians. Page 36, issue of July 7.

MAY 7-15 — International Congress of Military Medicine and Pharmacy. Page 501, issue of September 29.

MAY 15-16 — American Board of Obstetrics and Gynecology, Inc. Page 218.

MAY 15-19 — American Medical Association, St. Louis, Missouri.

JUNE 6, 7, 8 — Massachusetts Medical Society. Worcester.

JUNE 12-17 — Symposium on the Public-Health Significance of the Virus and Rickettsial Diseases. Page 125, issue of January 19.

JUNE 26-29 — National Tuberculosis Association. Page 936, issue of December 8.

SEPTEMBER — Boston Psychoanalytic Institute. Page 450, issue of September 22.

SEPTEMBER 11-15 — American Congress on Obstetrics and Gynecology. Page 938, issue of December 8.

SEPTEMBER 15-28 — Pan-Pacific Surgical Association. Page 863, issue of November 24.

FALL, 1939 — Temperature Symposium. Page 218.

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH

FEBRUARY 8 — Essex Sanatorium, Middleton. Clinic at 5 p. m. Dinner at 7 p. m. Speaker: Dr. Edward Churchill. Subject: Surgical Treatment of Pulmonary Suppuration.

MARCH 1 — Lynn Hospital. Clinic at 5 p. m. Dinner at 7 p. m. Speaker: Dr. John Rock. Subject: Endocrinology.

APRIL 5 — Addison Gilbert Hospital, Gloucester. Clinic at 5 p. m. Dinner at 7 p. m. Speaker: Dr. Ethan Allan Brown. Subject: Allergy.

MAY 10 — Annual meeting. Salem Country Club, Peabody.

SUFFOLK

MARCH 29 — Joint meeting with New England Pediatric Society, Boston Medical Library, 8:15 p. m. Program and speakers to be announced.

APRIL 26 — Annual meeting in conjunction with Boston Medical Library, at 8:15 p. m. Election of officers. Program and speakers to be announced.

WORCESTER

FEBRUARY 8 — Page 173, issue of January 26.

MARCH 8 — Worcester Memorial Hospital.

APRIL 12 — Worcester Hahnemann Hospital.

MAY 10 — Worcester Country Club — Annual meeting.

With the exception of the annual meeting in May, all the meetings begin with a supper at 6:30 p. m., which is followed at 7:30 p. m. by the business and scientific sessions.

BOOK REVIEWS

Cranio-Cerebral Injuries: Their diagnosis and treatment. Donald Munro. 412 pp. London, New York and Toronto: Oxford University Press, 1938. $4.00.

Dr. Donald Munro, surgeon-in-chief for neurological surgery at the Boston City Hospital, has long been interested in injuries to the central nervous system. His large clinic, from which he reports over 1000 cases, has been a source of intensive study on the results of cerebral trauma. In addition, in associated departments of the hospital, experimental work has been carried forward which has added to our knowledge of intracranial pathology. The book, in review, is a personal report of the patients observed by him and the deductions drawn therefrom. The literature surveyed, in addition to his own publications, is largely, although not entirely, that emanating from the Boston City Hospital. This, however, should not detract from the value of the publication for it is Dr. Munro's experiences and the conclusions which he has drawn from them that are of value.

The subject is extensively covered. Beginning with the fundamentals of cerebral physiopathology, the author considers the important questions of history and examination of patients, roentgenology, general principles of treatment, operative and non-operative treatment, complications of craniocerebral injuries, the complications due to necessary treatment, first-aid, convalescent care and a general survey of his mortality and morbidity statistics. In addition, there is a chapter on craniocerebral injuries in the newborn.

In the opinion of the reviewer, no book covers the subject as well as this one. It is a practical, straightforward account of what has often been considered a field of great uncertainty. With the increasing number of automobile accidents, surgeons are forced, more and more, to handle patients with injuries of this type. Should they follow the outline set down by Dr. Munro, their results, provided they have equal technical skill in operation, should be greatly improved over the results of a decade ago. There are, moreover, many practical hints for the general practitioner, who is the one that usually sees patients of this type first. The author stresses the importance of getting the patient to a hospital as soon as possible and of combating surgical "shock" before particular attention is given to the intracranial injury. As he states, if a patient cannot be moved or surgical shock is such that it becomes a serious factor, the patient is unlikely to survive even if operated on later. The value of absolute rest, the avoidance of early roentgenological examination, lumbar puncture, intravenous medication and intracranial operation are all considered in turn. One of the most

important parts of the book is the chapter on subdural hematomas, a traumatic condition which is often overlooked by general practitioners.

Although there are hints about convalescent care, one wishes the author had said more about the prevention of one of the most serious complications of intracranial injury, namely traumatic neurosis. Can traumatic neurosis be differentiated from a postconcussional syndrome? As many patients, moreover, have difficulties with accident and other forms of insurance, one would wish the author had said even more about this aspect of the subject. Although, perhaps, the aim of the book is to instruct surgeons, the general title *Cranio-Cerebral Injuries: Their diagnosis and treatment* would indicate that a wider expansion of the subject by the author was to be expected. It should be pointed out, moreover, that the surgeon is the one who is called on to give the reports to the insurance company and often to testify in court action.

It is hoped that in a second edition of this book, which is sure to be called for, an additional chapter summarizing the whole situation will be given. Without increasing the size of the book, it would seem to the reviewer that the last chapter containing so many case reports might either be shortened or these case reports put in smaller type, thus leaving room for a final summary.

Doctor Bradley Remembers. Francis B. Young. 522 pp. New York: Reynal & Hitchcock, 1938. $2.75.

This is a full-length novel by a well-known British author, who formerly practiced medicine. He is therefore fully familiar with the field of medical practice. The story briefly consists of the reminiscences of an old doctor just retiring from the practice of medicine. It depicts the education of a country doctor and his practice in a small English mining town. The character of Dr. Bradley is well drawn, as is that of his family and the young physician who comes to him as an apprentice. Any physician will read this novel with pleasure. It should be pointed out, however, that so far as the public is concerned, erroneous impressions of medicine might be drawn by books of this type. This is also true of another novel, recently widely read, by Dr. Cronin. Although all that is put into these books is probably true, too much emphasis is put on the unfavorable side of medical practice. Dr. Young's book, however, is not so much to be criticized along these lines as other recent publications.

Synopsis of Clinical Laboratory Methods. W. E. Bray. Second edition. 408 pp. St. Louis: C. V. Mosby Co., 1938. $4.50.

Today there are a great many so-called laboratory handbooks. Most everyone working in the laboratory makes certain modifications of existing methods. Often these are incorporated as a laboratory manual and eventually present themselves as a handbook. This particular text is weak in respect to the present-day methods of blood chemistry, and the section on hematology is too detailed. The book is set up in type that is unusually difficult to read, and there are a good many typographical errors.

Insulin: Its chemistry and physiology. Hans F. Jensen. 252 pp. New York: The Commonwealth Fund, 1938. $2.00.

Dr. Jensen has written a very comprehensive monograph, not only with adequate references to the literature, but with a critical survey that is extremely valuable, coming as it does from one of the important workers in this field. He treats of the chemistry, biochemistry and physiology of insulin in such a readable way that the reader is given an excellent general survey, even though the latter's training may not fit him to understand all the details.

For men who expect to use insulin intelligently and keep abreast of the literature, the book is extremely timely and, indeed, an almost indispensable background, unless one has followed the literature in detail from the beginning.

Urology. Daniel N. Eisendrath and Harry C. Rolnick. Fourth edition, entirely revised and reset. 1061 pp. Philadelphia, Montreal and London: J. B. Lippincott Co., 1938. $10.00.

The fact that this is the fourth edition of this book is evidence of its popularity in the past. The present edition has been brought up to date by the inclusion of added material such as the antiseptic action of sulfanilamide and mandelic acid, cystometry and excretion pyelography.

A new chapter on the medical aspects of nephritis is unfortunate because it has been impossible to do the subject justice in the allotted space. On the other hand the inclusion of a few pages on ailments of the urethra and bladder of women is to be commended.

The work as a whole forms a compendium of present urologic knowledge gleaned from a wide survey of the literature. It lacks, in too large measure, critical discussion based on the personal experience of the writers.

A Textbook of Biochemistry: For students of medicine and science. A. T. Cameron. Fifth edition. 414 pp. New York: The Macmillan Co., 1938. $4.00.

The fifth edition of this text has been completely revised. Rewritten to include the rapid progress in biochemistry in the past few years, it deals with biochemical problems in a most lucid and clear manner. Dr. Cameron has the happy faculty of being able to explain without too much effort the underlying principles of most of the biochemical phenomena: a welcome text, indeed, in a field where the problems appear most intricate and confusing.

The Seasonal Periodicity of Malaria and the Mechanism of the Epidemic Wave. Clifford A. Gill. 136 pp. London: J. & A. Churchill Ltd., 1938. 10s. 6d.

This modest little book on the epidemiology of malaria is unusually significant and, therefore, important.

In Part I, the author divides the world roughly into climatic zones of malaria. Each of these zones is characterized by stated features of temperature and of humidity which are significant with reference to the transmission of malaria. The epidemiological types of malaria in each of the four zones are discussed in Part II. The waves of malaria which occur in the spring and in the autumn or in both seasons are described. Part III, entitled "The General Properties of the Seasonal Wave," deals with its composition, periodicity, form, significance and mechanism. The last two chapters summarize some very important inferences which are well supported by the facts presented in the book.

The author points out that the anopheline factor and the meteorological factor, by reason of their influence on frequency of transmission, play important parts in the mechanism of the seasonal wave; but he believes that seasonal relapse is still more significant in the production of the seasonal wave. The cause of this pronounced tendency to seasonal relapse is still quite unknown.